JS 44 (Rev. 12/07)

# CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

**I. (a) PLAINTIFFS**
Hologic, Inc.
Cytyc Corporation
Hologic LP

E-FILING

**DEFENDANTS**
SenoRx, Inc.

**(b)** County of Residence of First Listed Plaintiff Middlesex County, MA
(EXCEPT IN U.S. PLAINTIFF CASES)

County of Residence of First Listed Defendant Orange County, CA
(IN U.S. PLAINTIFF CASES ONLY)
NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE LAND INVOLVED.

**(c)** Attorney's (Firm Name, Address, and Telephone Number)
Howrey LLP
1299 Pennsylvania Ave., NW
Washington, DC 20004
202-783-0800

ADR

C08 00133 MEJ

Attorneys (If Known)

**II. BASIS OF JURISDICTION** (Place an "X" in One Box Only)

- ☐ 1 U.S. Government Plaintiff
- ☒ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

**III. CITIZENSHIP OF PRINCIPAL PARTIES** (Place an "X" in One Box for Plaintiff and One Box for Defendant)
(For Diversity Cases Only)

| | PTF | DEF | | PTF | DEF |
|---|---|---|---|---|---|
| Citizen of This State | ☐ 1 | ☐ 1 | Incorporated *or* Principal Place of Business In This State | ☐ 4 | ☐ 4 |
| Citizen of Another State | ☐ 2 | ☐ 2 | Incorporated *and* Principal Place of Business In Another State | ☐ 5 | ☐ 5 |
| Citizen or Subject of a Foreign Country | ☐ 3 | ☐ 3 | Foreign Nation | ☐ 6 | ☐ 6 |

**IV. NATURE OF SUIT** (Place an "X" in One Box Only)

**CONTRACT**
- ☐ 110 Insurance
- ☐ 120 Marine
- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
- ☐ 151 Medicare Act
- ☐ 152 Recovery of Defaulted Student Loans (Excl. Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

**REAL PROPERTY**
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

**TORTS**

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury

PERSONAL INJURY
- ☐ 362 Personal Injury—Med. Malpractice
- ☐ 365 Personal Injury—Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

**CIVIL RIGHTS**
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 444 Welfare
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities – Other
- ☐ 440 Other Civil Rights

**PRISONER PETITIONS**
- ☐ 510 Motions to Vacate Sentence

Habeas Corpus:
- ☐ 530 General
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

**FORFEITURE/PENALTY**
- ☐ 610 Agriculture
- ☐ 620 Other Food & Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
- ☐ 640 R.R. & Truck
- ☐ 650 Airline Regs.
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

**LABOR**
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Mgmt. Relations
- ☐ 730 Labor/Mgmt.Reporting & Disclosure Act
- ☐ 740 Railway Labor Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Empl. Ret. Inc. Security Act

**IMMIGRATION**
- ☐ 462 Naturalization Application
- ☐ 463 Habeas Corpus – Alien Detainee
- ☐ 465 Other Immigration Actions

**BANKRUPTCY**
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

**PROPERTY RIGHTS**
- ☐ 820 Copyrights
- ☒ 830 Patent
- ☐ 840 Trademark

**SOCIAL SECURITY**
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

**FEDERAL TAX SUITS**
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

**OTHER STATUTES**
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Sat TV
- ☐ 810 Selective Service
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 890 Other Statutory Actions
- ☐ 891 Agricultural Acts
- ☐ 892 Economic Stabilization Act
- ☐ 893 Environmental Matters
- ☐ 894 Energy Allocation Act
- ☐ 895 Freedom of Information Act
- ☐ 900Appeal of Fee Determination Under Equal Access to Justice
- ☐ 950 Constitutionality of State Statutes

**V. ORIGIN** (Place an "X" in One Box Only)
☒ 1 Original Proceeding | ☐ 2 Removed from State Court | ☐ 3 Remanded from Appellate Court | ☐ 4 Reinstated or Reopened | ☐ 5 Transferred from another district (specify) | ☐ 6 Multidistrict Litigation | ☐ 7 Appeal to District Judge from Magistrate Judgment

**VI. CAUSE OF ACTION**
Cite the U.S. Civil Statute under which you are filing **(Do not cite jurisdictional statutes unless diversity):**
35 U.S.C. 271, et seq.
Brief description of cause:
Patent Infringement

**VII. REQUESTED IN COMPLAINT:**
☐ CHECK IF THIS IS A CLASS ACTION UNDER F.R.C.P. 23
DEMAND $0.00
CHECK YES only if demanded in complaint:
JURY DEMAND: ☒ Yes ☐ No

**VIII. RELATED CASE(S) IF ANY** (See instructions): JUDGE Whyte
DOCKET NUMBER U.S.D.C. - Northern Dist. Cal. San Jose Div. - CV 05-05312 RMW (RS)

DATE
January 8, 2008

SIGNATURE OF ATTORNEY OF RECORD

FOR OFFICE USE ONLY

RECEIPT # _____ AMOUNT _____ APPLYING IFP _____ JUDGE _____ MAG. JUDGE _____

# United States District Court

## NORTHERN DISTRICT OF CALIFORNIA

Hologic, Inc., Cytyc Corporation, and Hologic LP

E-FILING

**SUMMONS IN A CIVIL CASE**

CASE NUMBER:

**V.**

SenoRx, Inc.

ADR C08 00133 MEJ

TO: (Name and address of defendant)

SenoRx, Inc.
11 Columbia, Suite A
Aliso Viejo, CA 92656

**YOU ARE HEREBY SUMMONED** and required to serve upon PLAINTIFF'S ATTORNEY (name and address)

Henry C. Su
Howrey LLP
1950 University Avenue, 4th Floor
East Palo Alto, California 94303

an answer to the complaint which is herewith served upon you, within **20** days after service of this summons upon you, exclusive of the day of service. If you fail to do so, judgement by default will be taken against you for the relief demanded in the complaint. You must also file your answer with the Clerk of this Court within a reasonable period of time after service.

Richard W. Wieking
CLERK

JAN 0 8 2008
DATE

(BY) DEPUTY CLERK

Tiffany Salinas-Harwell

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Attorneys for Plaintiffs HOLOGIC, INC., CYTYC CORPORATION and HOLOGIC L.P.



UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

HOLOGIC, INC. CYTYC CORPORATION, and HOLOGIC L.P.,

Plaintiffs,

vs.

SENORX, INC.,

Defendant.

Case No. C08 00133 MEJ

**COMPLAINT FOR PATENT INFRINGEMENT SEEKING DAMAGES AND INJUNCTIVE RELIEF**

**DEMAND FOR JURY TRIAL**

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Attorneys for Plaintiffs HOLOGIC, INC., CYTYC CORPORATION and HOLOGIC L.P.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

| | |
|---|---|
| HOLOGIC, INC. CYTYC CORPORATION, and HOLOGIC L.P., Plaintiffs, vs. SENORX, INC., Defendant. | Case No. **COMPLAINT FOR PATENT INFRINGEMENT SEEKING DAMAGES AND INJUNCTIVE RELIEF** **DEMAND FOR JURY TRIAL** |

Plaintiffs Hologic, Inc., Cytyc Corporation, and Hologic L.P. (together, "Hologic"), by their attorneys, complain against SenoRx, Inc. ("SenoRx"), and allege as follows:

## NATURE OF THE ACTION

1. Hologic brings this action to seek damages and injunctive relief arising out of the infringement by SenoRx of U.S. Patent Nos. 5,913,813, 6,413,204, and 6,482,142 (together, the "Patents-In-Suit," attached hereto at Exhibits A, B, and C, respectively).

2. Plaintiff Hologic, Inc. is a Delaware corporation with a place of business at 35 Crosby Drive, Bedford, Massachusetts 01730.

3. Plaintiff Cytyc Corporation is a Delaware corporation with a place of business at 250 Campus Drive, Marlborough, Massachusetts 01752.

4. Plaintiff Hologic L.P. is a limited partnership with a place of business at 250 Campus Drive, Marlborough, Massachusetts 01752.

5. Defendant SenoRx is a Delaware corporation with a principal place of business at 11 Columbia, Aliso Viejo, California 92656.

## JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction over Hologic's claims of patent infringement pursuant to 28 U.S.C. § 1338(a) because the claims arise under the Patent Act, 35 U.S.C. § 281.

7. This Court has personal jurisdiction over SenoRx because, on information and belief, SenoRx regularly and systematically transacts business in this District.

8. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391(b), 1391(c) and 1400(b) because on information and belief, SenoRx has committed, and intends to commit, acts of infringement in this District.

## INTRADISTRICT ASSIGNMENT

9. This is an Intellectual Property Action within the meaning of the Court's Assignment Plan, and therefore is subject to assignment on a district-wide basis pursuant to Civil Local Rule 3-2(b).

## BACKGROUND

10. Hologic is a leading developer, manufacturer and supplier of premium diagnostic, therapeutic and medical imaging systems dedicated to serving the healthcare needs of women, and a leading developer of state-of-the-art digital imaging technology for general radiography and mammography applications. Hologic's business units are focused on mammography and breast biopsy, direct-to-digital x-ray for general radiography applications, treatment of breast cancer, cervical cancer screening gynecological surgery, osteoporosis assessment, and mini C-arm imaging for orthopedic applications. Each year, more than one million women are diagnosed with breast cancer, while hundreds of thousands of them fall victim to this dreaded disease. Hologic has achieved a leading market position in breast cancer detection in the United States.

11. Through its recently-acquired Cytyc subsidiary, Hologic has, *inter alia*, developed and marketed innovative radiation delivery systems for the treatment of cancer since 1995. One such system is the MammoSite® Radiation Therapy System, which delivers targeted, therapeutically effective doses of radiation directly to the breast tissue where cancer is most likely to recur. To affect this delivery of radiation, the MammoSite® System provides for the placement of a radiation source inside the human body, specifically within a cavity created in the breast tissue after the cancerous tumor has been removed.

12. The MammoSite® Radiation Therapy System has been widely used by radiation oncologists and breast surgeons to treat breast cancer patients who are undergoing breast conservation therapy. Breast conservation therapy involves excising only the cancerous tumor in a surgical procedure known as a lumpectomy and preserving the healthy breast tissue, including the nipple, the skin, the fatty tissue underneath and the pectoral muscle. Because this operation does not remove the entire breast (as is the case with a total mastectomy), there is a chance that some pre-cancerous and/or cancerous cells remain at the margins of excision and therefore the cancer may return. Accordingly, it is recommended that patients undergo certain post-operative treatments such as chemotherapy and radiation therapy to eliminate or minimize the likelihood that the cancer will recur.

13. The term brachytherapy refers to radiation therapy in which the radiation source is placed in proximity to the tissue being treated and contrasts with the use of an external radiation

source, which irradiates a wider area of the body that includes the tissue to be treated. Because it places the radiation source within the cavity created by the lumpectomy, in proximity to the tissue that surrounded the cancerous tumor, the MammoSite® Radiation Therapy System provides a treatment method referred to as breast brachytherapy. The placement of the radiation source at the lumpectomy site is achieved through the use of a balloon catheter applicator.

14. In May 2002, Proxima Therapeutics, Inc. ("Proxima Therapeutics") obtained clearance from the U.S. Food and Drug Administration ("FDA") to market the MammoSite® Radiation Therapy System as a new medical device. Proxima Therapeutics was a pioneer in breast radiation therapy and made significant investments in the research, development and testing of therapeutically effective devices and methods for implementing breast brachytherapy, including the Mammosite® system.

15. To protect those investments, Proxima Therapeutics applied for and obtained a number of patents, including U.S. Patent Nos. 5,913,813, 6,413,204, and 6,482,142, which are the subject of this Complaint.

16. In 2005, Proxima Therapeutics was acquired by Cytyc Corporation, and, in 2007, Hologic, Inc. combined with Cytyc Corporation. Cytyc Corporation is the assignee and owner of U.S. Patent Nos. 5,913,813, 6,413,204, and 6,482,142, which are the subject of this Complaint.

17. On information and belief, SenoRx submitted a premarket notification under Section 510(k) of the Food, Drug and Cosmetic Act to the FDA for its device for implementing breast brachytherapy, to be marketed under the name SenoRad Multi-Lumen Balloon Source Applicator For Brachytherapy (the "SENORAD MULTI-LUMEN BALLOON"). As required by Section 510(k), SenoRx had to persuade the FDA that its device is a substantial equivalent to an already approved and classified medical device.

18. The FDA approved SenoRx's premarket notification on or about May 18, 2007, as evidenced by the Section 510(k) summary (No. K071229), a true and correct copy of which is attached as Exhibit D. The FDA determined that there is substantial equivalence between SenoRx's SENORAD MULTI-LUMEN BALLOON and Hologic's patented MammoSite® Radiation Therapy System. The notification states: "The SenoRad applicator has the following similarities to the previously cleared predicate devices: same indications for use; same intended use; same intended

treatment site; ***same operating principle; same technological characteristics; equivalent dosimetric characteristics***; and same sterilization method. The materials of construction vary in a manner that has no impact on device safety. In summary, the SenoRad Multi-Lumen Balloon Source Applicator as described in this submission is substantially equivalent to the predicate devices." (*See* Exhibit D (emphasis added).)

19. On information and belief, SenoRx has given the SenoRad device the commercial moniker the "Contura™ Multi-Lumen Balloon."

**COUNT ONE – INFRINGEMENT OF U.S. PATENT NO. 5,913,813**

20. Hologic incorporates by reference its allegations in Paragraphs 1-19 above.

21. On information and belief, and based on likely evidentiary support after a reasonable opportunity for further investigation or discovery, SenoRx is presently making, using, offering for sale, and/or selling a device for implementing brachytherapy (including, without limitation, the Contura™ Multi-Lumen Balloon) that infringes one or more claims of U.S. Patent No. 5,913,813 (the "'813 patent"), literally or under the doctrine of equivalents. A true and correct copy of the '813 patent is attached as Exhibit A.

22. On information and belief, and based on likely evidentiary support after a reasonable opportunity for further investigation or discovery, SenoRx is presently inducing or contributing to the infringement of one or more claims of the '813 patent.

23. Such activities by SenoRx as described in Paragraphs 18 and 19 above, if proven, violate one or more subsections of 35 U.S.C. § 271.

24. On information and belief, SenoRx's infringement of the '813 patent has been willful and wanton because SenoRx has had notice of the '813 patent.

25. If SenoRx's infringing activities are not preliminarily and permanently enjoined, Hologic will suffer irreparable harm that cannot be adequately compensated by a monetary award.

26. Hologic has suffered economic harm as a result of SenoRx's infringing activities in an amount to be proven at trial.

**COUNT TWO – INFRINGEMENT OF U.S. PATENT NO. 6,413,204**

27. Hologic incorporates by reference its allegations in Paragraphs 1-26 above.

28. On information and belief, and based on likely evidentiary support after a reasonable opportunity for further investigation or discovery, SenoRx is presently making, using, offering for sale, selling a device for implementing brachytherapy (including, without limitation, the Contura™ Multi-Lumen Balloon) that infringes one or more claims of U.S. Patent No. 6,413,204 (the "'204 patent"), literally or under the doctrine of equivalents. A true and correct copy of the '204 patent is attached as Exhibit B.

29. On information and belief, and based on likely evidentiary support after a reasonable opportunity for further investigation or discovery, SenoRx is presently inducing or contributing to the infringement of one or more claims of the '204 patent.

30. Such activities by SenoRx as described in Paragraphs 25 and 26 above, if proven, violate one or more subsections of 35 U.S.C. § 271.

31. On information and belief, SenoRx's infringement of the '204 patent has been willful and wanton because SenoRx has had notice of the '204 patent.

32. If SenoRx's infringing activities are not preliminarily and permanently enjoined, Hologic will suffer irreparable harm that cannot be adequately compensated by a monetary award.

33. Hologic has suffered economic harm as a result of SenoRx's infringing activities in an amount to be proven at trial.

**COUNT THREE – INFRINGEMENT OF U.S. PATENT NO. 6,482,142**

34. Hologic incorporates by reference its allegations in Paragraphs 1-33 above.

35. On information and belief, and based on likely evidentiary support after a reasonable opportunity for further investigation or discovery, SenoRx is presently making, using, offering for sale, selling a device for implementing brachytherapy (including, without limitation, the Contura™ Multi-Lumen Balloon) that infringes one or more claims of U.S. Patent No. 6,482,142 (the "'142 patent"), literally or under the doctrine of equivalents. A true and correct copy of the '142 patent is attached as Exhibit C.

36. On information and belief, and based on likely evidentiary support after a reasonable opportunity for further investigation or discovery, SenoRx is presently inducing or contributing to the infringement of one or more claims of the '142 patent.

37. Such activities by SenoRx as described in Paragraphs 32 and 33 above, if proven, violate one or more subsections of 35 U.S.C. § 271.

38. On information and belief, SenoRx's infringement of the '142 patent has been willful and wanton because SenoRx has had notice of the '142 patent.

39. If SenoRx's infringing activities are not preliminarily and permanently enjoined, Hologic will suffer irreparable harm that cannot be adequately compensated by a monetary award.

40. Hologic has suffered economic harm as a result of SenoRx's infringing activities in an amount to be proven at trial.

## DEMAND FOR JURY TRIAL

41. Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure and Civil Local Rule 3-6(a), Hologic hereby demands a trial by jury on all issues so triable.

## PRAYER FOR RELIEF

WHEREFORE, Hologic prays that this Court grant it the following relief:

(a) enter judgment against SenoRx adjudging the '204, '142, and '813 patents to be valid, enforceable and infringed;

(b) issue a preliminary and permanent injunction against SenoRx for infringement of the '204, '813, and '142 patents pursuant to 35 U.S.C. § 283;

(c) award Hologic an amount adequate to compensate for SenoRx's infringement of the Patents-In-Suit, as provided under 35 U.S.C. § 284;

(d) an adjudication that SenoRx has willfully infringed the Patents-In-Suit and increasing the award of damage to Hologic up to three times in view of SenoRx's willful infringement;

(e) a declaration that this is an exceptional case under 35 U.S.C. § 285 and that Hologic be awarded its attorneys' fees and costs incurred in prosecuting their claims as provided under 35 U.S.C. § 285; and

(f) such other relief as this Court deems proper.

Dated: January 8, 2008

HOWREY LLP

By: _____
Henry C. Su

Attorneys for Plaintiffs
Hologic, Inc.,
Cytyc Corporation and
Hologic L.P.

# EXHIBIT A

US005913813A

# United States Patent [19]

**Williams et al.**

[11] **Patent Number: 5,913,813**

[45] **Date of Patent: Jun. 22, 1999**

[54] **DOUBLE-WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE**

[75] Inventors: **Jeffery A. Williams**, Baltimore, Md.; **Christopher H. Porter**, Woodinville, Wash.; **Jeffrey F. Williamson**; **James F. Dempsey**, both of St. Louis, Mo.; **Timothy J. Patrick**; **James B. Stubbs**, both of Alpharetta, Ga.

[73] Assignee: **Proxima Therapeutics, Inc.**, Alpharetta, Ga.

[21] Appl. No.: **08/900,021**

[22] Filed: **Jul. 24, 1997**

[51] **Int. Cl.**[6] ..... **A61N 5/00**

[52] **U.S. Cl.** ..... **600/3**

[58] **Field of Search** ..... 600/1–8

[56] **References Cited**

U.S. PATENT DOCUMENTS

| | | | |
|---|---|---|---|
| 3,324,847 | 6/1967 | Zoumboulis . | |
| 5,106,360 | 4/1992 | Ishiwara et al. . | |
| 5,429,582 | 7/1995 | Williams . | |
| 5,611,767 | 3/1997 | Williams . | |
| 5,662,580 | 9/1997 | Bradshaw et al. | 600/3 |
| 5,782,742 | 7/1998 | Crocker et al. . | |
| 5,785,688 | 7/1998 | Joshi et al. . | |

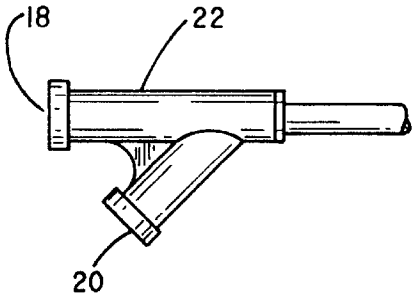
*Primary Examiner*—John P. Lacyk

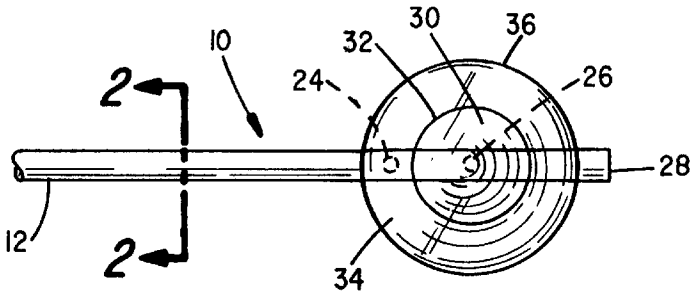
*Attorney, Agent, or Firm*—Nikolai, Mersereau & Dietz, P.A.

[57] **ABSTRACT**

An instrument for use in brachytherapy comprises a concentric arrangement of inner and outer distensible, spherical chambers disposed near the proximal end of a catheter body where one of the chambers is made to contain a radioactive material with the other chamber containing a radiation absorptive material, the apparatus functioning to provide a more uniform absorbed dose profile in tissue surrounding a cavity created by the removal of a tumor. An alternative embodiment includes non-spherical inner and outer chambers whose respective walls are spaced equidistant over the entire surfaces thereof.

**13 Claims, 2 Drawing Sheets**



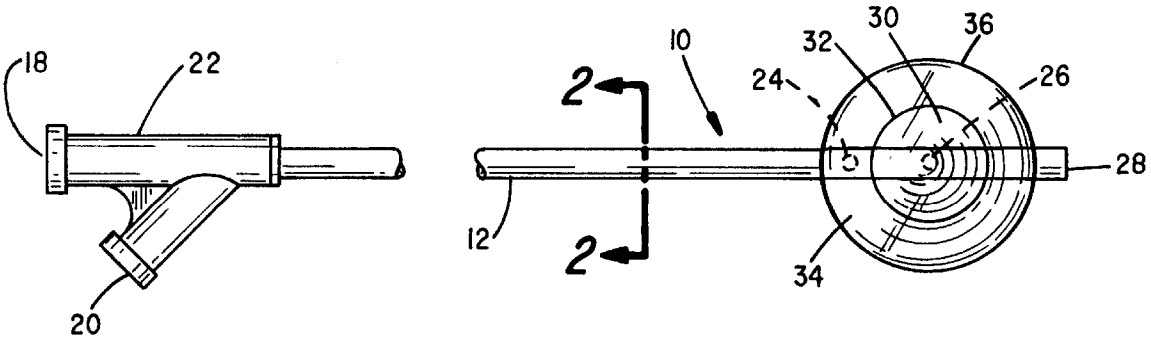



FIG. 1

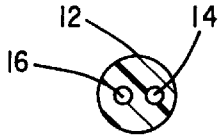



FIG. 2

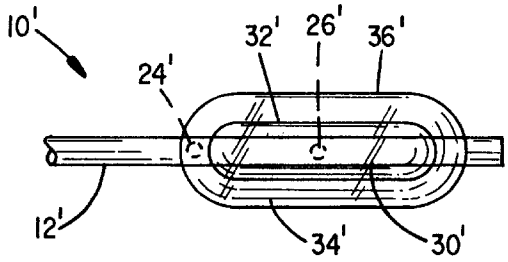



FIG. 3

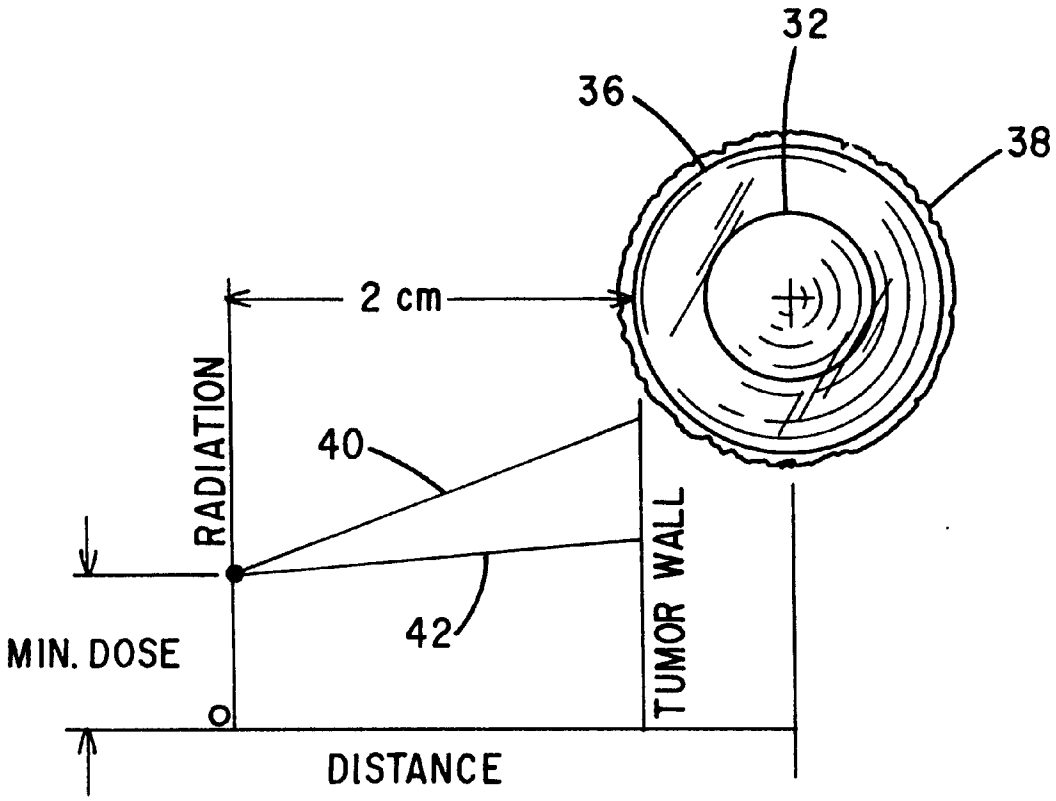



FIG. 4

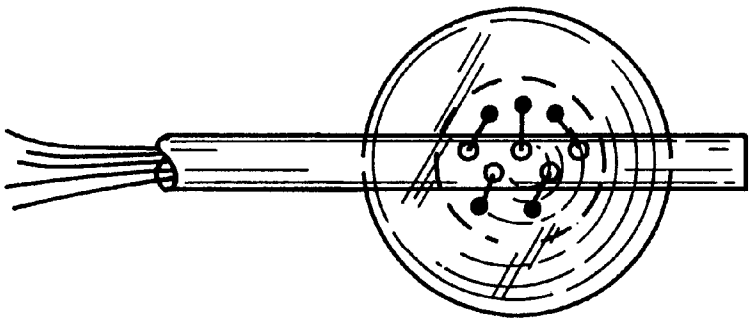


FIG. 5

# DOUBLE-WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE

## BACKGROUND OF THE INVENTION

I. Field of the Invention

This invention relates generally to apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radioactive material and/or radiation emissions.

II. Discussion of the Prior Art

In the Williams U.S. Pat. No. 5,429,582 entitled "Tumor Treatment", there is described a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the margins surrounding the excised tumor. In accordance with that patent, there is provided a catheter having an inflatable balloon at a distal end thereof to define a distensible reservoir. Following surgical removal of a tumor, say in the brain or breast, the deflated balloon may be introduced into the surgically-created pocket left following removal of a tumor and then the balloon is inflated by injecting a fluid having radionuclide(s) therein into the distensible reservoir, via a lumen in the catheter.

When it is considered that the absorbed dose rate at a point exterior to the radioactive source is inversely proportional to the square of the distance between the radiation source and the target point, tissue directly adjacent the wall of the distensible reservoir may be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a site 0–3 cms away from the wall of the excised tumor. It is desirable to keep the radiation in the space between that site and the wall of the distensible reservoir as uniform as possible to prevent over-exposure to tissue at or near the reservoir wall. In treating other cancers, such as bladder cancer, where the neoplastic tissue is generally located on the bladder surface, deep penetration is unnecessary and to be avoided.

A need exists for an instrument which may be used to deliver radiation from a radioactive source to target tissue within the human body of a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target.

## SUMMARY OF THE INVENTION

We have found that it is possible to deliver a desired radiation dose at a predetermined radial distance from a source of radioactivity by providing a first spacial volume at the distal end of a catheter and a second spacial volume defined by a surrounding of the first spatial volume by a polymeric film wall where the distance from the spatial volume and the wall is maintained substantially constant over their entire surfaces. One of the inner and outer volumes is filled with either a fluid or a solid containing a radionuclide(s) while the other of the two volumes is made to contain either a low radiation absorbing material, e.g., air or even a more absorptive material, such as an x-ray contrast fluid. Where the radioactive material comprises the core, the surrounding radiation absorbing material serves to control the radial profile of the radioactive emissions from the particular one of the inner and outer volumes containing the radionuclide(s) so as to provide a more radially uniform radiation dosage in a predetermined volume surrounding the outer chamber. Where the core contains the absorbent material, the radial depth of penetration of the radiation can be tailored by controlling the core size.



## DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. **1** is a side view of an apparatus for delivering radioactive emissions to body tissue;

FIG. **2** is a cross-sectional view taken along the line **2**—**2** in FIG. **1**;

FIG. **3** is a fragmentary side view of an apparatus for administering radiation therapy in accordance with a second embodiment;

FIG. **4** is a graph helpful in understanding the operation of the apparatus of the present invention; and

FIG. **5** depicts a further embodiment of the invention.

## DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring first to FIG. **1**, there is indicated generally by numeral **10** a surgical instrument for providing radiation treatment to proliferative tissue in a living patient. It is seen to comprise a tubular body member **12** having first and second lumens **14** and **16** (FIG. **2**) extending from proximal ports **18** and **20** in a molded plastic hub **22** to inflation ports **24** and **26** formed through the side wall of the tube **12** and intersecting with the lumens **14** and **16**, respectively.

Affixed to the tubular body **12** proximate the distal end **28** thereof is an inner spatial volume **30** which may be defined by a generally spherical polymeric film wall **32**. The interior of the chamber **30** is in fluid communication with the inflation port **26**. Surrounding the spatial volume **30** is an outer chamber **34** defined by an outer polymeric film wall **36** that is appropriately spaced from the wall **32** of the inner chamber **30** when the two chambers are inflated or otherwise filled and supported. Chamber **34** encompasses the inflation port **24**.

The embodiment of FIG. **1** can be particularly described as comprising two spherical chambers **30** and **34**, one inside the other. In accordance with a first embodiment of the invention, the outer chamber **34**, being the volume defined by the space between the inner spherical wall **32** and the outer spherical wall **36**, may be filled with air or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. The inner chamber **30** is then filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles or other therapeutic rays.

Those skilled in the art will appreciate that instead of having the inner spatial volume **30** defined by a generally spherical polymeric film wall as at **32**, the catheter body member **12** may have a solid spherical radiation emitting material in which event that solid sphere would be surrounded with the outer spherical wall **36** with the spatial volume therebetween occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

It is further contemplated that instead of having the inner spatial volume comprising a single solid sphere, it may instead comprise a plurality of radioactive particles strategically placed within the inner spatial volume so as to radiate

in all directions with a substantially equal intensity. FIG. **5** illustrates a catheter having the inner spatial volume occupied by a plurality of radioactive beads that are mounted on the distal ends of a plurality of wires that are routed through the catheter body and exit a plurality of ports formed through the wall of the catheter body and reaching the lumen. This arrangement allows the exact positioning of the individual radiation sources to be positioned so as to generate a desired resultant profile.

It is not essential to the invention that the chambers **30** and **34** have spherical walls, so long as the spacing between the wall of the inner chamber and the wall of the outer chamber remain generally constant, such as is illustrated in FIG. **3**.

Referring to FIG. **4**, there is shown the two concentric spherical chambers of FIG. **1** defined by inner spherical wall **32** and outer spherical wall **36** disposed within the margin **38** of a surgically excised tumor. It is desired that the radiation emitted from the core **32** be capable of delivering a certain minimum dose absorbed at a location approximately 0–3 cms from the margin **38**. Curve **40** is a plot of absorbed dose vs. radial distance that would be obtained if the inner chamber defined by spherical wall **32** was not present and the entire volume of the spherical chamber defined by wall **36** were filled with the radioactive fluid. Plot **42** reflects the absorbed dose distribution as a function of radial distance when the radioactive fluid is contained within the inner chamber and is surrounded by either a gas or a more radiation absorbing material. Comparing the plots **40** and **42**, by providing the concentric arrangement depicted, the absorbed dose profile in the space between the 2 cm site and the wall of the outer balloon is maintained much more uniform, thus preventing over-treatment of body tissue at or close to the outer wall **36** of the instrument. That is to say, to obtain the same end point absorbed dose at 2 cm, it would be necessary to increase the source activity relative to that used for a completely filled (to surface **36**) configuration, assuming the same radionuclide is used in both configurations.

With no limitation intended, the distensible polymeric chambers may comprise a biocompatible, radiation resistant polymer, such as Silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, PVC, C-Flex. The radioactive fluid contained within the inner chamber **32** can be made from any solution of radionuclide(s), e.g., a solution of I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel.

In the embodiments heretofore described, the material containing the radionuclide(s) is located in the inner chamber. The invention also contemplates that the outer chamber **34** may contain the material having the radionuclide therein while the inner chamber **30** contains the radiation absorptive material. This configuration is advantageous where a profile exhibiting higher intensity at a tissue surface with lesser penetration is desired. By using this approach, less volume of radioactive material is required than if the entire volume of the device were filled with radioactive material. Moreover, the outer chamber wall need not be spherical, yet a uniform profile is obtainable. Experiments have shown that a steeper radial absorbed source gradient can be obtained using a radiation attenuation fluid in the inner chamber **30** than otherwise obtains when only a single distensible chamber is used, as in the aforereferenced Williams U.S. Pat. No. 5,429,582. The invention also contemplates that the radioactive material in the inner core can be replaced by a core containing solid radionuclide-containing particles. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used in place of the fluid. This radioactive source can either be preloaded into the catheter at the time of manufacture or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. Such a solid radioactive core configuration offers the advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources.

In either the concentric spherical embodiment of FIG. **1** or the non-spherical configuration of FIG. **3**, the spacing between the inner and outer chambers needs to be held somewhat constant to avoid "hot spots". This result can be achieved by careful placement of precision blown polymer parisons or by using compressible foams or mechanical spacers in the form of webs joining the inner wall **32** to the outer wall **36**.

This invention has been described herein in considerable detail in order to comply with the patent statutes and to provide those skilled in the art with the information needed to apply the novel principles and to construct and use such specialized components as are required. However, it is to be understood that the invention can be carried out by specifically different equipment and devices, and that various modifications, both as to the equipment and operating procedures, can be accomplished without departing from the scope of the invention itself.

What is claimed is:

**1**. Apparatus for delivering radioactive emissions to a body location with a uniform radiation profile, comprising:

(a) a catheter body member having a proximal end and distal end;

(b) an inner spatial volume disposed proximate the distal end of the catheter body member;

(c) an outer, closed, inflatable, chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;

(d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and

(e) means disposed in the other of the inner spatial volume and outer chamber for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides.

**2**. The apparatus as in claim **1** wherein said inner spatial volume is an inner closed, chamber defined by a further radiation transparent wall.

**3**. The apparatus of claim **1** wherein the means for rendering uniform the absorbed dose profile is a radiation attenuating material.

**4**. The apparatus of claim **3** wherein the radiation attenuating material is selected from a group consisting of barium sulphate, water, and X-ray contrast media.

**5**. The apparatus as in claim **2** wherein the radionuclide is in a fluid form.

**6**. The apparatus as in claim **5** wherein the fluid comprises an isotope of iodine.

**7**. The apparatus as in claim **1** wherein the radionuclide is a slurry of a fluid containing particles of a solid isotope.

**8**. The apparatus as in claim **2** wherein the inner chamber contains the radioactive material.

**9**. The apparatus as in claim **1** wherein the outer chamber contains the radioactive material.

**10**. The apparatus as in claim **8** wherein the radioactive material is a fluid.

**11**. The apparatus as in claim **8** wherein the radioactive material is a solid.



**12**. The apparatus as in claim **1** wherein the material containing a radionuclide comprises a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile.

**13**. The apparatus as in claim **2** wherein the inner and outer chambers are spherical in shape and are concentric.

* * * * *

# EXHIBIT B

(12) **United States Patent**
**Winkler et al.**

(10) **Patent No.: US 6,413,204 B1**
(45) **Date of Patent: *Jul. 2, 2002**

(54) **INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES**

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(73) Assignee: **Proxima Therapeutics, Inc.**, Alpharetta, GA (US)

( * ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **09/293,524**

(22) Filed: **Apr. 15, 1999**

**Related U.S. Application Data**

(63) Continuation-in-part of application No. 08/900,021, filed on Jul. 4, 1997, now Pat. No. 5,913,813.

(51) **Int. Cl.**[7] ..... **A61N 5/00**
(52) **U.S. Cl.** ..... **600/3**
(58) **Field of Search** ..... 600/1–8

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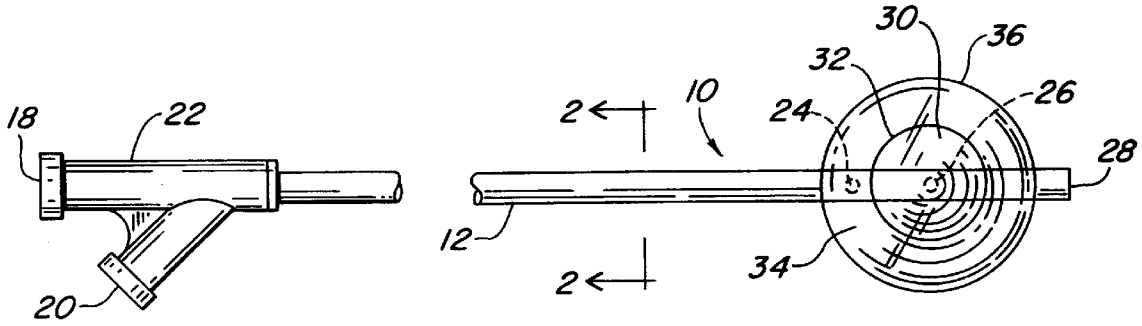
*Primary Examiner*—John P. Lacyk
(74) *Attorney, Agent, or Firm*—Thomas J. Engellenner; Ronald E. Cahill; Nutter, McClennen & Fish, LLP

(57) **ABSTRACT**

An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location includes a catheter body member having a proximal end and distal end, an inner spatial volume disposed proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume, and a radiation source disposed in the inner spatial volume.

**36 Claims, 3 Drawing Sheets**



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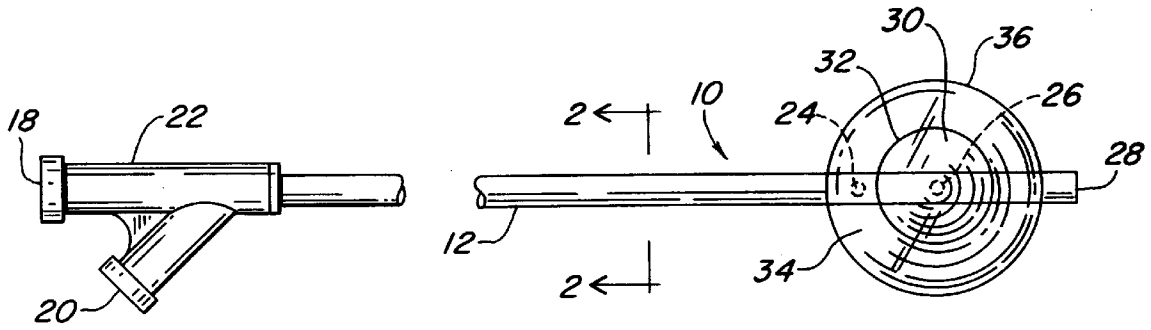


FIG. 1

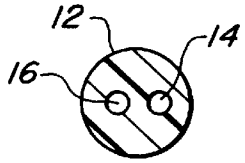


FIG. 2

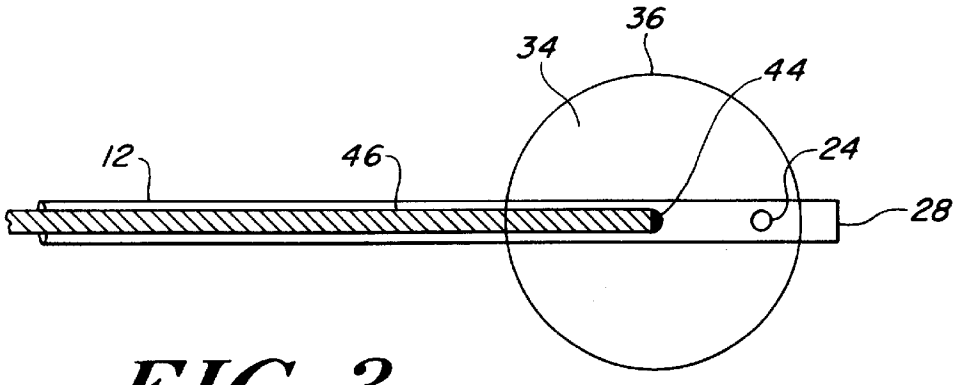


FIG. 3

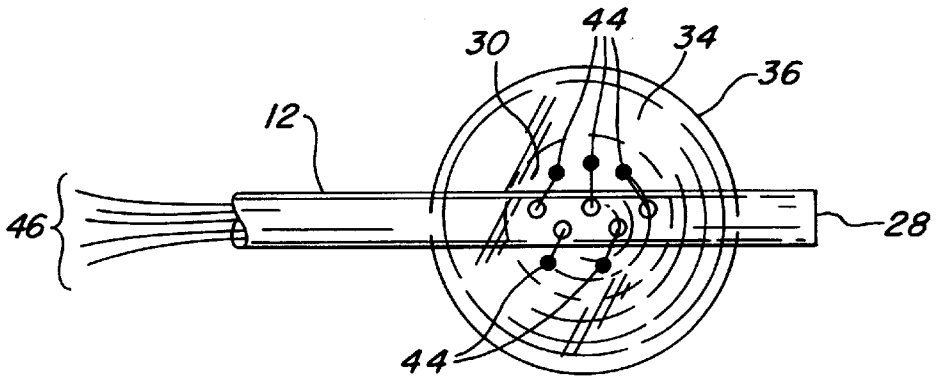


FIG. 4

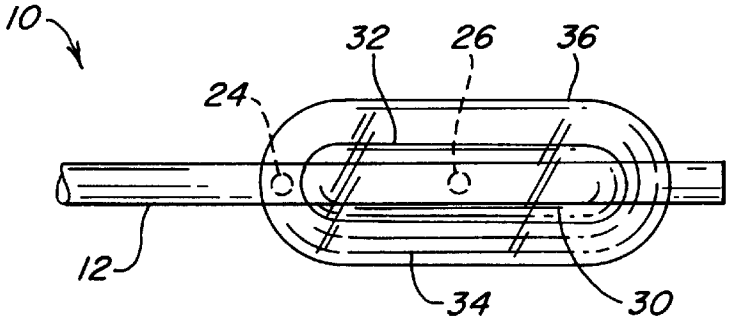


FIG. 5

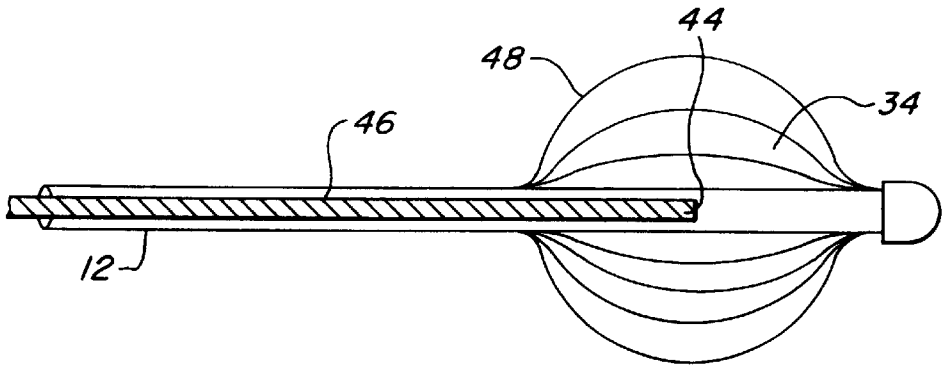


FIG. 6

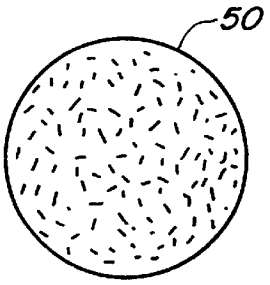


FIG. 7A

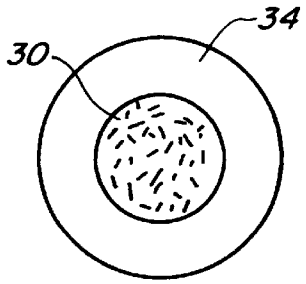


FIG. 7B

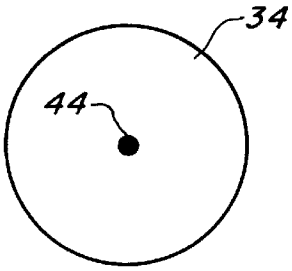


FIG. 7C

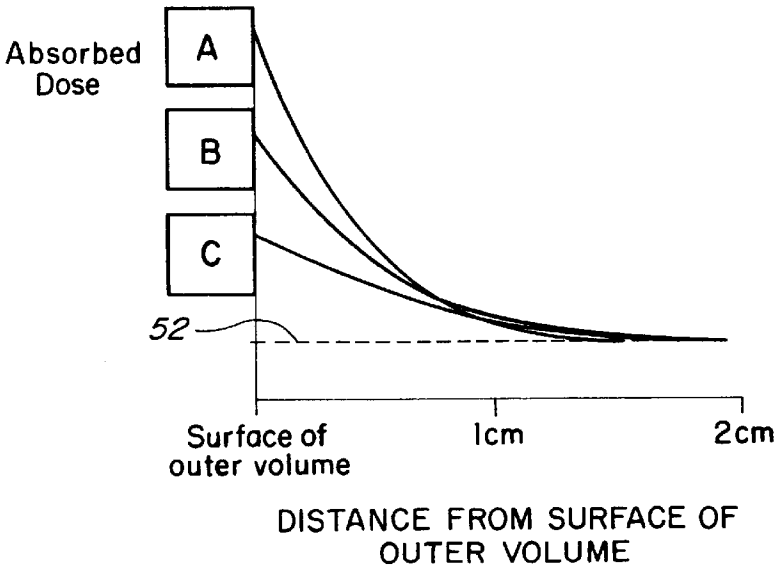


FIG. 7D

# INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES

## CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. patent application Ser. No. 08/900,021, filed Jul. 24, 1997, now U.S. Pat. No. 5,913,813 the contents of which are specifically incorporated herein by reference.

## BACKGROUND OF THE INVENTION

The invention relates generally to apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radiation.

Malignant tumors are often treated by surgical resection of the tumor to remove as much of the tumor as possible. Infiltration of the tumor cells into normal tissue surrounding the tumor, however, can limit the therapeutic value of surgical resection because the infiltration can be difficult or impossible to treat surgically. Radiation therapy can be used to supplement surgical resection by targeting the residual tumor margin after resection, with the goal of reducing its size or stabilizing it. Radiation therapy can be administered through one of several methods, or a combination of methods, including external-beam radiation, stereotactic radiosurgery, and permanent or temporary interstitial brachytherapy. The term "brachytherapy," as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. Owing to the proximity of the radiation source, brachytherapy offers the advantage of delivering a more localized dose to the target tissue region.

For example, brachytherapy is performed by implanting radiation sources directly into the tissue to be treated. Brachytherapy is most appropriate where 1) malignant tumor regrowth occurs locally, within 2 or 3 cm of the original boundary of the primary tumor site; 2) radiation therapy is a proven treatment for controlling the growth of the malignant tumor; and 3) there is a radiation dose-response relationship for the malignant tumor, but the dose that can be given safely with conventional external beam radiotherapy is limited by the tolerance or normal tissue. In brachytherapy, radiation doses are highest in close proximity to the radiotherapeutic source, providing a high tumor dose while sparing surrounding normal tissue. Interstitial brachytherapy is useful for treating malignant brain and breast tumors, among others.

Interstitial brachytherapy is traditionally carried out using radioactive seeds such as $^{125}I$ seeds. These seeds, however, produce inhomogeneous dose distributions. In order to achieve a minimum prescribed dosage throughout a target region of tissue, high activity seeds must be used, resulting in very high doses being delivered in some regions in proximity to the seed or seeds which can cause radionecrosis in healthy tissue.

Williams U.S. Pat. No. 5,429,582, entitled "Tumor Treatment," describes a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the tissue surrounding the excised tumor. In order to implement the radioactive emissions, Williams provides a catheter having an inflatable balloon at its distal end that defines a distensible reservoir. Following surgical removal of a tumor, the surgeon introduces the balloon catheter into the surgically created pocket left following removal of the tumor. The balloon is then inflated by injecting a fluid having one or more radionuclides into the distensible reservoir via a lumen in the catheter.



The apparatus described in Williams solves some of the problems found when using radioactive seeds for interstitial brachytherapy, but leaves some problems unresolved. The absorbed dose rate at a target point exterior to a radioactive source is inversely proportional to the square of the distance between the radiation source and the target point. As a result, where the radioactive source has sufficient activity to deliver a prescribed dose, say 2 centimeters into the target tissue, the tissue directly adjacent the wall of the distensible reservoir, where the distance to the radioactive source is very small, may still be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a region up to about two centimeters away from the wall of the excised tumor. It is desirable to keep the radiation that is delivered to the tissue in the target treatment region within a narrow absorbed dose range to prevent over-exposure to tissue at or near the reservoir wall, while still delivering the minimum prescribed dose at the maximum prescribed distance from the reservoir wall.

There is still a need for an instrument which can be used to deliver radiation from a radioactive source to target tissue within the human body with a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target.

## SUMMARY OF THE INVENTION

The present invention solves the problems described above by providing an interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location. The apparatus includes a catheter body member having a proximal end and distal end, an inner spatial volume disposed proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume, and a radiation source disposed in the inner spatial volume. The inner and outer spatial volumes are configured to provide an absorbed dose within a predetermined range throughout a target tissue. The target tissue is located between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface. The predetermined dose range is defined as being between a minimum prescribed absorbed dose for delivering therapeutic effects to tissue that may include cancer cells, and a maximum prescribed absorbed dose above which healthy tissue necrosis may result.

In different embodiments, the inner spatial volume can be defined by a distensible polymeric wall containing radioactive source material which can be a fluid material, by a solid radioactive source, or by a region containing a plurality of solid radioactive sources. The outer spatial volume is defined by an expandable surface element that may be, for example, an inflatable polymeric wall or an expandable cage. The expandable surface element can cause tissue to conform to its intended shape, and preferably, the apparatus creates absorbed isodose profiles in the target tissue that are substantially similar in shape to the expandable surface element in substantially three dimensions.

The invention also provides a method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location. The method includes surgically creating access to the proliferating tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue. An interstitial brachytherapy apparatus for delivering radioactive emissions as described above is then provided and intra-operatively placed into the resection cavity. After a prescribed absorbed dose has been delivered to tissue surrounding the apparatus, the apparatus is removed. The radioactive source material may be placed into the interstitial brachytherapy apparatus after the apparatus is placed in the resection cavity, and may be removed before the apparatus is removed. The method has particular applications to brain and breast cancers.

## DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. **1** is a side view of an interstitial brachytherapy apparatus of the invention for delivering radioactive emissions to body tissue;

FIG. **2** is a cross-sectional view taken along the line **2**—**2** in FIG. **1**;

FIG. **3** is an additional embodiment of an interstitial brachytherapy apparatus of the invention having a solid radiation source;

FIG. **4** is an additional embodiment of an interstitial brachytherapy apparatus of the invention having a radiation source comprising a plurality of solid radiation particles;

FIG. **5** depicts a further embodiment of the invention wherein the inner and outer spatial volumes of the interstitial brachytherapy apparatus are non-spherical;

FIG. **6** illustrates an interstitial brachytherapy apparatus of the invention having an expandable outer spatial volume surface; and

FIGS. **7**A–D illustrate the absorbed dose versus distance into target tissue for several interstitial brachytherapy apparatus configurations.

## DESCRIPTION OF THE PREFERRED EMBODIMENT

A surgical instrument **10** for providing radiation treatment to proliferative tissue in a living patient is illustrated in FIG. **1**. Surgical instrument **10** includes a tubular body member **12** having first and second lumens **14** and **16** (FIG. **2**) extending from proximal ports **18** and **20** in a molded plastic hub **22** to inflation ports **24** and **26** formed through the side wall of the tube **12** and intersecting with the lumens **14** and **16**, respectively.

Affixed to the tubular body **12** proximate the distal end **28** thereof is an inner spatial volume **30** which may be defined by a generally spherical polymeric film wall **32**. The interior of the inner volume **30** is in fluid communication with the inflation port **26**. Surrounding inner spatial volume **30** is an outer spatial volume **34** defined by an outer polymeric film wall **36** that is appropriately spaced from the wall **32** of the inner spatial volume **30** when the two volumes are inflated or otherwise supported. Outer volume **34** encompasses inflation port **24**. With no limitation intended, the distensible polymeric film walls may comprise a biocompatible, radiation resistant polymer, such as silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, or PVC.



The embodiment of FIG. **1** includes inner and outer spatial volumes **30** and **34**, one inside the other. The outer spatial volume **34**, being the volume defined by the space between the inner spherical wall **32** and the outer spherical wall **36**, may be filled with air or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. The inner volume **30** is then filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material contained within the inner chamber **32** can be a fluid made from any solution of radionuclide(s), e.g., a solution of I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel. One radioactive material useful in the invention is Iotrex™, a sterile single use, non-pyrogenic solution containing sodium 3-($^{125}$I)iodo-4-hydroxybenzenesulfonate ($^{125}$I-HBS), available from Proxima Therapuetics, Inc. of Alpharetta, Ga.

As an alternative method of providing radioactive source material, such material may be coated on, chemically bonded to, or copolymerized with the material forming inner spherical wall **32**.

Where the radioactive source material is provided as a fluid or gel within inner spherical wall **32**, it may be desirable to provide a solid outer spherical wall **36**. Should inner spherical wall **32** rupture, the radioactive source material will be retained within outer spherical wall **36** and will not leak into the patient. For further safety, the burst strength of inner spherical wall **32** may be designed so as to be lower than that of outer spherical wall **36**. In this way, inner spherical wall **32** will rupture under stress first, releasing its contents into the larger combined space of the inner and outer volumes **30**, **34** and releasing any pressure built up within the inner spherical wall **32** and reducing the risk that radioactive material will spill into the patient. In the event of such a rupture, radioactive fluid could be drained from the apparatus through port **24** by way of lumen **14**, and also from port **26** by way of lumen **16**.

In a further embodiment, illustrated in FIG. **3**, instead of having the inner spatial volume **30** defined by a generally spherical polymeric film wall as at **32**, the catheter body member **12** may have a solid spherical radiation emitting material **44** as the inner spatial volume **30**. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used. This radioactive source can either be preloaded into the catheter at the time of manufacture or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. The solid radiation emitting material **44** can be inserted through catheter **12** on a wire **46**, for example, using an afterloader (not shown). Such a solid radioactive core configuration offers an advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources. In this embodiment solid spherical inner spatial volume **30** is surrounded by outer spherical wall **36**, defining outer spatial volume **34** between the outer spherical wall **36** and the inner spatial volume **30** with the outer spatial volume **34** occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

In a further embodiment, illustrated in FIG. **4**, inner spatial volume **30**, instead of comprising a single solid sphere, may comprise a plurality of radiation emitting particles **44** strategically placed within the inner spatial volume **30** so as to radiate in all directions with a substantially equal intensity. This plurality of radiation emitting particles **44** can be mounted on the distal ends of a plurality of wires **46** that are routed through the catheter body **12** and exit a plurality of ports formed through the wall of the catheter body and reaching the lumen. This arrangement allows the exact positioning of the individual radiation sources **44** to be positioned so as to generate a desired resultant profile.

As illustrated in FIG. **5**, it is not essential to the invention that the volumes **30** and **34** have spherical walls, so long as the resultant dosing profile is consistent with the shape of the outer volume **34**. That is, the absorbed dose within the target tissue at points equidistant from the surface **36** of the outer spatial volume **34** should be substantially uniform in substantially every direction. Put another way, the three dimensional isodose profiles generated by the radiation source should be substantially similar in shape to the outer spatial volume **34**. Where the inner and outer spatial volumes are created by inflatable membranes and one of the volumes contains a fluid radiation source, this can be achieved by ensuring that the spacing between the wall of the inner volume and the wall of the outer volume remain generally constant. In either the concentric spherical embodiment of FIG. **1** or the non-spherical configuration of FIG. **5**, this result can be achieved by careful placement of precision blown or molded polymer partitions or by using compressible foams or mechanical spacers in the form of webs joining the inner wall **32** to the outer wall **36**. The desired isodose profiles conforming to the shape of the outer spatial volume **34** can also be obtained, for example, by strategic placement of a plurality of radioactive particle sources within the inner spatial volume **30**. Where the apparatus of the invention is deployed in soft tissue, it may also be important for the surface **36** of the outer spatial volume **34** to be sufficiently firm so as to force the target tissue to take on the shape of the surface **36** so that the desired relationship between the isodose profiles and the target tissue is achieved.

When used in an interstitial application, the surface of the outer spatial volume **34** must establish a relationship between the inner spatial volume **30** and the target tissue so as to achieve the aforementioned isodose profile, however, the surface of the outer volume need not be a solid material. For example, as illustrated in FIG. **6**, the surface of the outer volume **34** could be an expandable cage **48** formed from a shape memory metal, such as nitinol, or a suitable plastic, such as an expandable polyethylene cage. Such a cage can be formed in the desired shape to conform to a particular isodose profile, then be contracted for delivery to the target site in vivo, then expanded to cause the tissue surrounding the surgically resected region to take the appropriate shape. The size of the outer spatial volume **34** generally will correspond approximately to the amount of tissue resected, or be slightly larger, allowing the expandable surface of the outer spatial volume to urge tissue on the surface of the resected region into the appropriate shape to promote an even dose distribution around the outer spatial volume in the target tissue. In typical applications, the outer spatial volume has a diameter of approximately 2 to 4 centimeters. In these same applications, where the radiation source is provided as a fluid within an inner balloon, the inner balloon generally has a diameter of approximately 0.5 to 3 centimeters.

FIGS. **7**A–D illustrate the ability of an interstitial brachytherapy apparatus of the invention to deliver a minimum prescribed dose within target tissue while avoiding necrosis inducing radiation "hot spots" in tissue proximate to the apparatus. FIG. **7**A illustrates an interstitial brachytherapy apparatus (device A) such as those employed in U.S. Pat. No. 5,429,582, having a single spatial volume **50** filled with a radioactive material in solution. FIG. **7**B illustrates an interstitial brachytherapy apparatus (device B) of the invention having a first, inner spatial volume **30** filled with a radioactive material in solution and defined by membrane **32**, and a second, outer spatial volume **34** defined by membrane **36** that is substantially evenly spaced apart from membrane **32** in substantially three dimensions. FIG. **7**C illustrates an additional interstitial brachytherapy apparatus (device C) of the invention having a solid, spherical radiation source **44** as the inner spatial volume and a spherical outer spatial volume **34** defined by membrane **36**.

Each of the devices illustrated in FIGS. **7**A–C can be configured to deliver a substantially uniform dose at a given distance into the target tissue from the surface of the outer spatial volume **34** (or from single spatial volume **50** for device A) and to deliver a minimum prescribed dose within a given prescribed depth range into the tissue from the surface of the outer spatial volume **34**. However, the different devices provide very different dose profiles as a function of distance from the surface of the outer volume as illustrated in FIG. **7**D. FIG. **7**D plots the absorbed dose at a given distance into the target tissue from the surface of the outer spatial volume **34** for each of the devices A, B, and C.

Each device can deliver a minimum prescribed dose **52** at a given distance from the surface of the outer spatial volume. For example, device A can readily be configured to provide a dose in a therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall. In a typical embodiment, the radioactive source material ranges from approximately 150 to 450 mCi in activity and encompasses most of the target treatment area with a 0.4 to 0.6 Gray/hour isodose contour. At this treatment rate, treatment may be completed in approximately 3 to 7 days, or more commonly, in approximately 3 to 5 days.

In order to reach the minimum prescribed dosage at this distance, however, device A must provide a dose proximate to the surface of the outer spatial volume that is substantially larger than the minimum prescribed dose. For the 4.0 cm diameter outer spatial volume example, the absorbed dosage would be approximately 131 Gray at the outer spatial volume surface. Ideally, radiation therapy should make use the inherent difference in radiosensitivity between the tumor and the adjacent normal tissues to destroy cancerous tissue while causing minimal disruption to surrounding normal tissues. At high doses of radiation, however, the percentage of exposed cells that survive treatment decreases with first-order kinetics in proportion to increasing radiation dose. With increasing cell death comes increasing risk of necrosis or tissue death in healthy tissue that is treated with a high dose of radiation. Accordingly, it is desirable to keep the maximum radiation dose delivered by the brachytherapy apparatus as low as possible while still delivering the desired therapeutic dose to the desired range of tissue.

Comparing the plots A, B, and C, the absorbed dose profile in the space between the 2 cm site and the surface of the outer spatial volume for the devices of the invention is maintained in a much narrower range, preventing over-treatment of body tissue at or close to the surface of the outer volume of the device. Because devices B and C provide an outer spatial volume **34** between the radioactive source and

the target tissue, these devices can use hotter radiation sources to reach the minimum prescribed dosage, but take advantage of the distance between the radioactive source and the target tissue provided by the outer spatial volume **34** to reduce or eliminate hot spots in the target tissue.

Returning to the 4.0 cm diameter outer spatial volume example, if the radiation source is contained within an inner spatial volume, say a solid radioactive sphere such as device C, the absorbed dose profile becomes much different. If the radiation source is configured to provide the same 60 Gray dose at 0.5 cm into the target tissue, the absorbed dose at the outer spatial volume surface is only 94 Gray—a significant decrease from the 131 Gray dose for a type A device. In addition, the treatment range for the type C device will be extended under these circumstance as compared to the type A device, delivering a 40 Gray dose beyond 1.0 cm into the target tissue and delivering approximately double the dose at 3.0 cm into the target tissue. In one embodiment, the inner and outer spatial volumes are configured to control the absorbed dose at the outer spatial volume surface so that the absorbed dose is no greater than about 100 Gray while providing a therapeutic absorbed dose into the target tissue at the desired range. The capability of the apparatus of the invention to deliver absorbed doses deeper into the target tissue than prior interstitial brachytherapy devices while controlling the dose in proximity to the apparatus to reduce or eliminate the risk of healthy tissue necrosis allows for the use of brachytherapy in a greater number of cases.

The interstitial brachytherapy apparatus of the invention can be used in the treatment of a variety of malignant tumors, and is especially useful for in the treatment of brain and breast tumors.

Many breast cancer patients are candidates for breast conservation surgery, also known as lumpectomy, a procedure that is generally performed on early stage, smaller tumors. Breast conservation surgery is typically followed by postoperative radiation therapy. Studies report that 80% of breast cancer recurrences after conservation surgery occur near the original tumor site, strongly suggesting that a tumor bed "boost" of local radiation to administer a strong direct dose may be effective in killing any remaining cancer and preventing recurrence at the original site. Numerous studies and clinical trials have established equivalence of survival for appropriate patients treated with conservation surgery plus radiation therapy compared to mastectomy.

Surgery and radiation therapy are the standard treatments for malignant solid brain tumors. The goal of surgery is to remove as much of the tumor as possible without damaging vital brain tissue. The ability to remove the entire malignant tumor is limited by its tendency to infiltrate adjacent normal tissue. Partial removal reduces the amount of tumor to be treated by radiation therapy and, under some circumstances, helps to relieve symptoms by reducing pressure on the brain.

A method according to the invention for treating these and other malignancies begins by surgical resection of a tumor site to remove at least a portion of the cancerous tumor and create a resection cavity. Following tumor resection, but prior to closing the surgical site, the surgeon intraoperatively places an interstitial brachytherapy catheter apparatus, having an inner spatial volume and an outer spatial volume as described above but without having the radioactive source material loaded, into the tumor resection cavity. Once the patient has sufficiently recovered from the surgery, the interstitial brachytherapy catheter is loaded with a radiation source. The radioactive source dwells in the catheter until the prescribed dose of radiotherapy is delivered, typically for approximately a week or less. The radiation source is then retrieved and the catheter is removed. The radiation treatment may end upon removal of the brachytherapy apparatus, or the brachytherapy may be supplemented by further doses of radiation supplied externally.

It will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention. All references cited herein are expressly incorporated by reference in their entirety.

What is claimed is:

**1**. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

(a) a catheter body member having a proximal end and distal end;

(b) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

**2**. The apparatus of claim **1**, wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

**3**. The apparatus of claim **2**, wherein a predetermined spacing is provided between said inner spatial volume and the expandable surface element.

**4**. The apparatus of claim **3**, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element.

**5**. The apparatus of claim **2**, wherein the minimum prescribed absorbed dose is 40 Gray at a distance of at least one centimeter from the expandable surface element.

**6**. The apparatus of claim **5**, wherein the dose rate in at least a portion of the target tissue is between about 0.4 and 0.6 Gray/hour.

**7**. The apparatus of claim **5**, wherein the maximum absorbed dose delivered to the target tissue is less than 100 Gray.

**8**. The apparatus of claim **2**, wherein the outer spatial volume has a diameter between about two and four centimeters.

**9**. The apparatus of claim **2**, wherein the inner spatial volume is an inner closed, distensible chamber defined by a further radiation transparent wall.

**10**. The apparatus of claim **9**, wherein the radioactive source is in a fluid form.

**11**. The apparatus of claim **10**, wherein the expandable surface element is a solid distensible surface and the outer spatial volume is a closed, distensible chamber and the expandable surface element is a radiation transparent wall.

12. The apparatus of claim 11, wherein a burst strength of the distensible chamber defining the outer spatial volume is greater than a burst strength of the chamber defining the inner spatial volume.

13. The apparatus of claim 1, wherein the expandable surface element is an expandable cage.

14. The apparatus of claim 13, wherein the expandable cage comprises a shape memory material.

15. The apparatus of claim 14, wherein the expandable cage comprises nitinol.

16. The apparatus of claim 1, wherein the radiation source is a solid radiation source.

17. The apparatus of claim 1, wherein the radiation source is a plurality of solid radiation sources arranged to provide an isodose profile having a shape substantially similar to the shape of the outer spatial volume.

18. The apparatus of claim 2, wherein the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions.

19. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

(a) surgically creating access to the proliferating tissue in a patient;

(b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

(c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:

(i) a catheter body member having a proximal end and distal end;

(ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(iv) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element;

(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity until a prescribed absorbed dose has been delivered to tissue surrounding the apparatus; and

(e) removing the interstitial brachytherapy apparatus.

20. The method of claim 19, further including placing the radioactive source into the interstitial brachytherapy apparatus after the step of placing the apparatus into the tumor resection cavity.

21. The method of claim 19, further including removing the radioactive source from the interstitial brachytherapy apparatus before the step of removing the apparatus.

22. The method of claim 19, wherein the proliferating tissue is a patient's brain.

23. The method of claim 19, wherein the proliferating tissue is a patient's breast.

24. The method of claim 19, further including configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

25. The method of claim 24, further including providing a predetermined spacing between said inner spatial volume and the expandable surface element.

26. The method of claim 25, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element.

27. The method of claim 24, wherein the minimum prescribed absorbed dose is 40 Gray at a distance of at least one centimeter from the expandable surface element.

28. The method of claim 27, wherein the dose rate in at least a portion of the target tissue is between about 0.4 and 0.6 Gray/hour.

29. The method of claim 27, wherein the maximum absorbed dose delivered to the target tissue is less than 100 Gray.

30. The method of claim 24, wherein the outer spatial volume has a diameter between about two and four centimeters.

31. The method of claim 24, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

32. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

(a) surgically creating access to the proliferating tissue in a patient;

(b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

(c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:

(i) a catheter body member having a proximal end and distal end;

(ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(iv) a radiation source disposed in the inner spatial volume;

(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;

(e) configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface; and

(f) removing the interstitial brachytherapy apparatus.

33. The method of claim 32, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

34. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

(a) surgically creating access to the proliferating tissue in a patient;

(b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

(c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:

(i) a catheter body member having a proximal end and distal end;

(ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(iv) a radiation source disposed in the inner spatial volume;

(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;

(e) adapting the expandable surface element to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of the expandable surface element;

(f) delivering a prescribed absorbed dose to tissue surrounding the apparatus; and

(g) removing the interstitial brachytherapy apparatus.

**35**. The method of claim **34**, wherein the step of adapting the expandable surface element includes expanding the outer surface volume.



**36**. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

(a) a catheter body member having a proximal end and distal end;

(b) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(d) a radiation source disposed in the inner spatial volume;

wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

* * * * *

# EXHIBIT C

(12) **United States Patent**
**Winkler et al.**

(10) **Patent No.: US 6,482,142 B1**
(45) **Date of Patent: Nov. 19, 2002**

(54) **ASYMMETRIC RADIATION DOSING APPARATUS AND METHOD**

(75) Inventors: **Rance A. Winkler**, Atlanta; **Timothy J. Patrick**, Alpharetta, both of GA (US)

(73) Assignee: **Proxima Therapeutics, Inc.**, Alpharetta, GA (US)

( * ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/464,727**

(22) Filed: **Dec. 16, 1999**

**Related U.S. Application Data**

(63) Continuation-in-part of application No. 09/293,524, filed on Apr. 15, 1999, which is a continuation-in-part of application No. 08/900,021, filed on Jul. 24, 1997, now Pat. No. 5,913,813.

(51) **Int. Cl.**[7] ..... **A61N 5/00**
(52) **U.S. Cl.** ..... **600/3**
(58) **Field of Search** ..... 600/1–8

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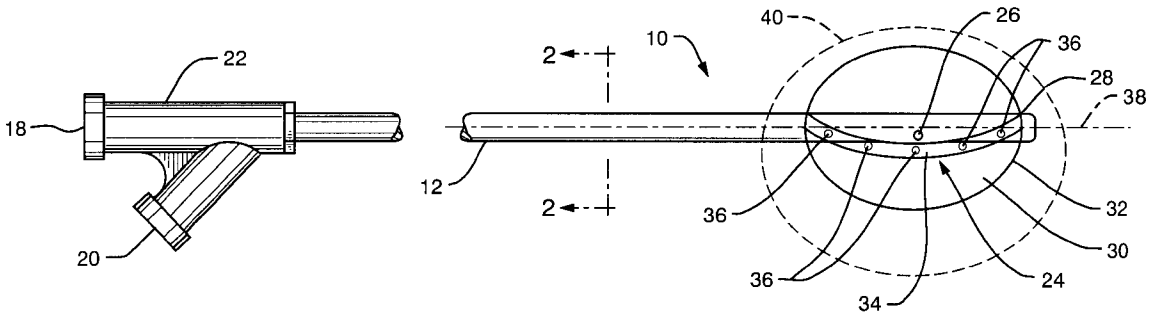
*Primary Examiner*—John P. Lacyk
(74) *Attorney, Agent, or Firm*—Thomas J. Engellenner; Ronald E. Cahill; Nutter McClennen & Fish LLP

(57) **ABSTRACT**

An interstitial brachytherapy apparatus of the invention delivers radioactive emissions in an asymmetric fashion to target tissue surrounding a surgical extraction site. The apparatus includes an expandable outer surface element defining an apparatus spatial volume, a radiation source disposed within the apparatus volume, and a means for providing predetermined asymmetric isodose curves within the target tissue. In one configuration, asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a longitudinal axis of the apparatus. In other configurations, asymmetric radiopaque shielding is provided between the radiation source and the target tissue. A surgical procedure using the apparatus is also described.

**14 Claims, 4 Drawing Sheets**



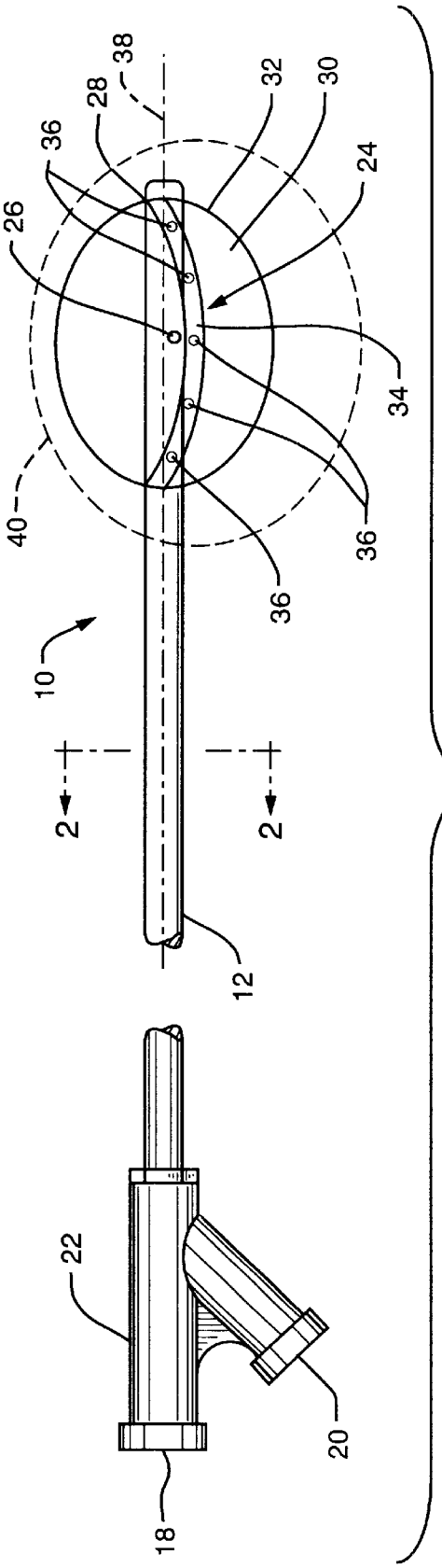



FIG. 1

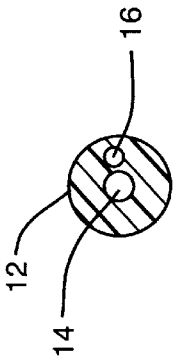



FIG. 2

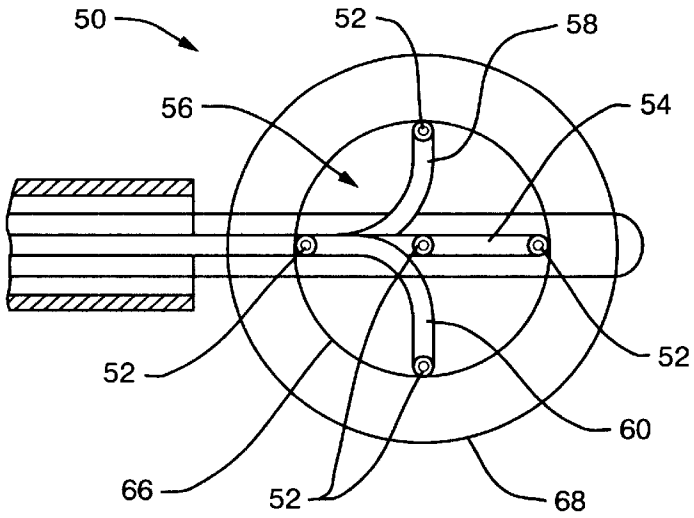



FIG. 3

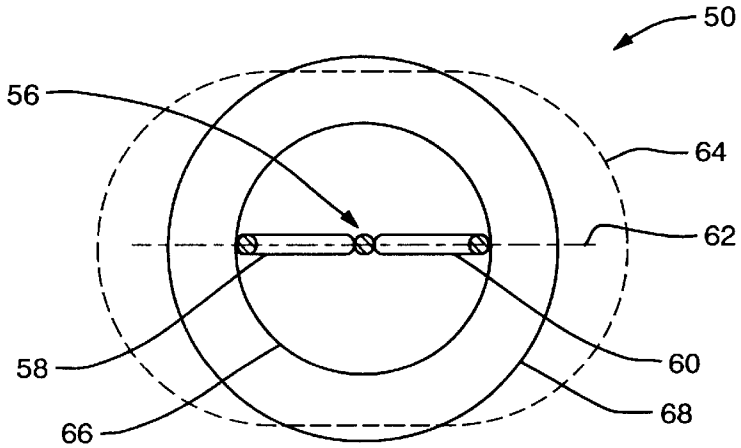



FIG. 3A

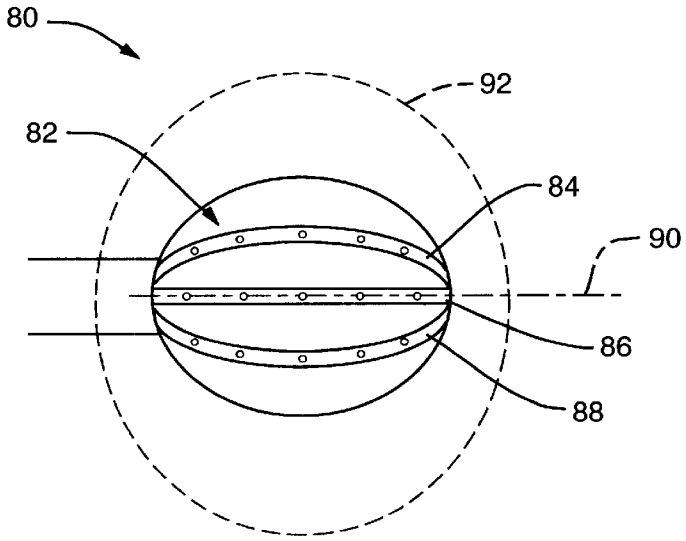
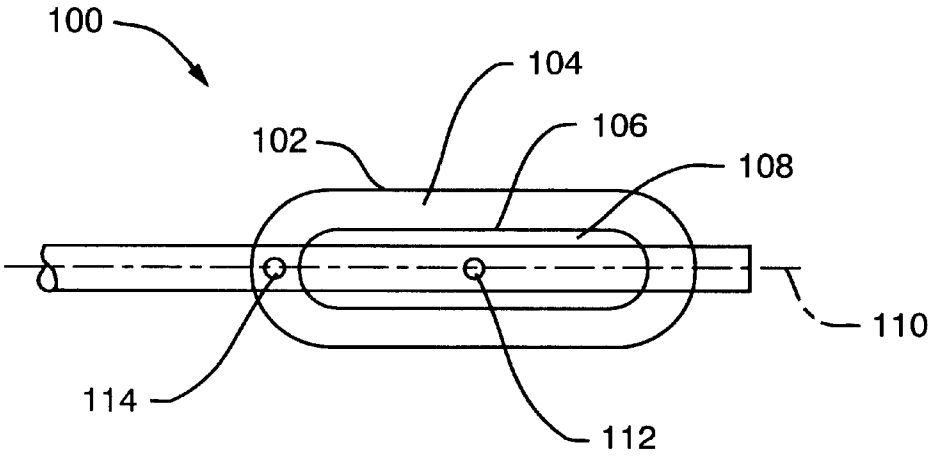



FIG. 4


100
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112

FIG. 5

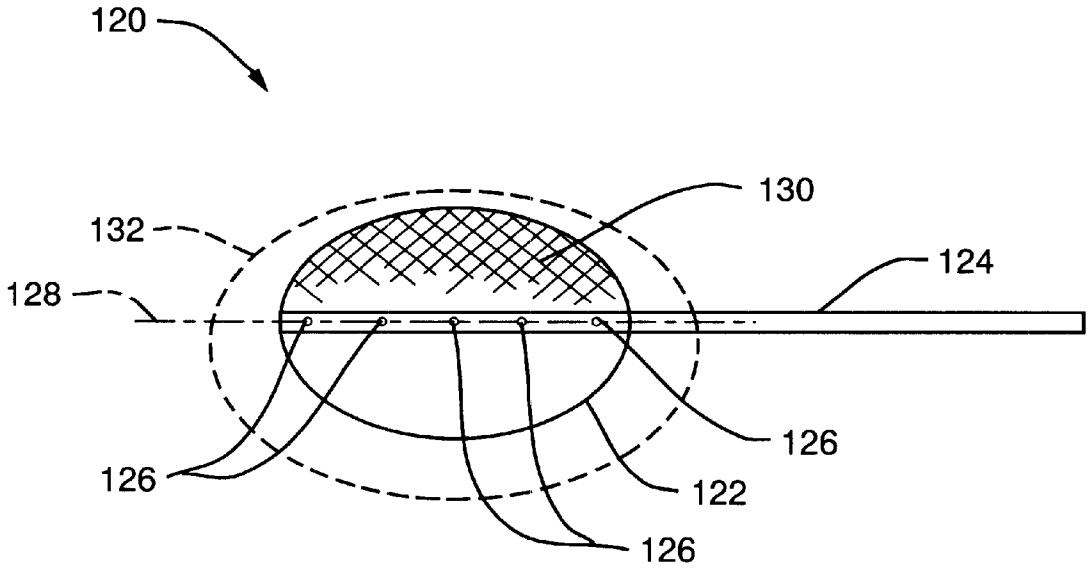
120
130
132
124
128
126
126
122
126

FIG. 6

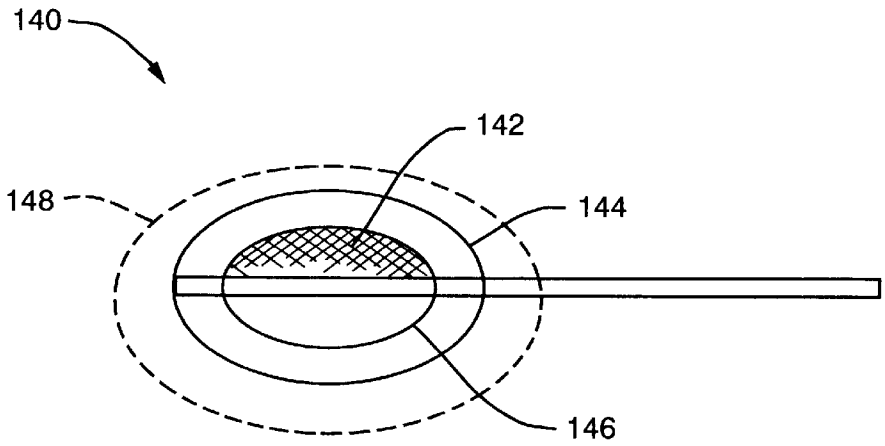


FIG. 7

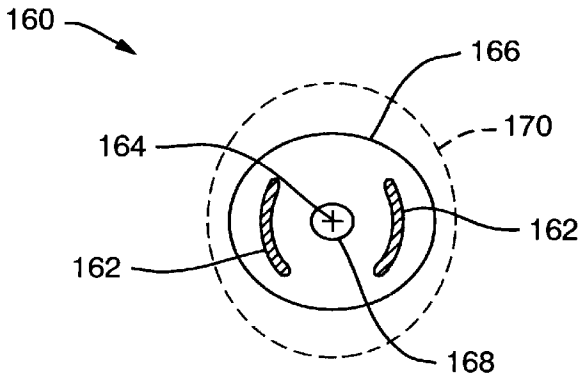


FIG. 8

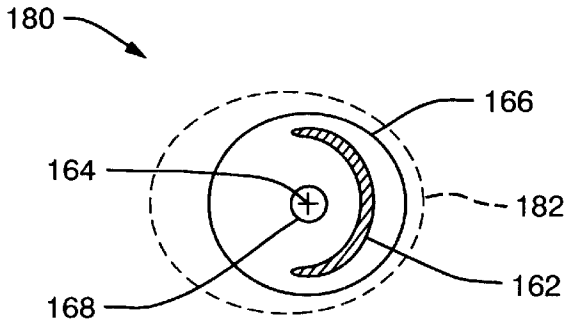


FIG. 9

# ASYMMETRIC RADIATION DOSING APPARATUS AND METHOD

## CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of co-pending U.S. patent application Ser. No. 09/293,524, filed Apr. 15, 1999, pending which is a continuation-in-part U.S. patent application Ser. No. 08/900,021, filed Jul. 24, 1997 (now issued as U.S. Pat. No. 5,913,813 to Williams et al.); the contents of these applications are specifically incorporated herein by reference.

## BACKGROUND OF THE INVENTION

The, invention relates generally to an apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radiation.

Malignant tumors are often treated by surgical resection of the tumor to remove as much of the tumor as possible. Infiltration of the tumor cells into normal tissue surrounding the tumor, however, can limit the therapeutic value of surgical resection because the, infiltration can be difficult or impossible to treat surgically. Radiation therapy can be used to supplement surgical resection by targeting the residual tumor margin after resection, with the goal of reducing its size or stabilizing it. Radiation therapy can be administered through one of several methods, or a combination of methods, including external-beam radiation, stereotactic radiosurgery, and permanent or temporary interstitial brachytherapy. The term "brachytherapy," as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. Owing to the proximity of the radiation source, brachytherapy offers the advantage of delivering a more localized dose to the target tissue region.

For example, brachytherapy is performed by implanting radiation sources directly into the tissue to be treated. Brachytherapy is most appropriate where 1) malignant tumor regrowth occurs locally, within 2 or 3 cm of the original boundary of the primary tumor site; 2) radiation therapy is a proven treatment for controlling the growth of the malignant tumor; and 3) there is a radiation dose-response relationship for the malignant tumor, but the dose that can be given safely with conventional external beam radiotherapy is limited by the tolerance or normal tissue. In brachytherapy, radiation doses are highest in close proximity to the radiotherapeutic source, providing a high tumor dose while sparing surrounding normal tissue. Interstitial brachytherapy is useful for treating malignant brain and breast tumors, among others.

Interstitial brachytherapy is traditionally carried out using radioactive seeds such as $^{125}I$ seeds. These seeds, however, produce inhomogeneous dose distributions. In order to achieve a minimum prescribed dosage throughout a target region of tissue, high activity seeds must be used, resulting in very high doses being delivered in some regions in proximity to the seed or seeds which can cause radionecrosis in healthy tissue. One attempt to address this problem, at least with respect to limiting dosages to critical organs near the radioactive seed site, has been to provide a shield directly on a portion of the seed or on an applicator that holds the seed to shield the particularly sensitive tissue. (E.g., Nath et al., Development of an $^{241}Am$ Applicator for Intracavitary Irradiation of Gynecologic Cancers, *Intl. J. Radiation Oncology Biol. Phys.*, Vol., 14, pp. 969–978.) While this approach may be appropriate for some applications, it may still be overly "hot" for treating proximate tissue on the unshielded side of the seed, while not providing an effective dose on the shielded side of the seed.



Williams U.S. Pat. No. 5,429,582, entitled "Tumor Treatment," describes a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the tissue surrounding the excised tumor. In order to implement the radioactive emissions, Williams provides a catheter having an inflatable balloon at its distal end that defines a distensible reservoir. Following surgical removal of a tumor, the surgeon introduces the balloon catheter into the surgically created pocket left following removal of the tumor. The balloon is then inflated by injecting a fluid having one or more radionuclides into the distensible reservoir via a lumen in the catheter.

The apparatus described in Williams solves some of the problems found when using radioactive seeds for interstitial brachytherapy, but leaves some problems unresolved. The absorbed dose rate at a target point exterior to a radioactive source is inversely proportional to the square of the distance between the radiation source and the target point. s a result, where the radioactive source has sufficient activity to deliver a prescribed dose, say 2 centimeters into the target tissue, the tissue directly adjacent the wall of the distensible reservoir, where the distance to the radioactive source is very small, may still be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a region up to about two centimeters away from the wall of the excised tumor. It is desirable to keep the radiation that is delivered to the tissue in the target treatment region within a narrow absorbed dose range to prevent over-exposure to tissue at or near the reservoir wall, while still delivering the minimum prescribed dose at the maximum prescribed distance from the reservoir wall. It is also desirable, at least in some applications, to provide these advantages while tailoring the radiation dosage to avoid fully dosing sensitive tissue or to reduce the amount of radiation that escapes the patient's body.

There its still a need for an instrument which can be used to deliver radiation from a radioactive source to target tissue within the human body with a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target, and with the ability to shape the radiation dose to protect sensitive tissue or to protect against radiation exposure outside of the patient's body which may affect healthcare providers or others who might come close to the patient.

## SUMMARY OF THE INVENTION

The present invention solves the problems described above by providing an interstitial brachytherapy apparatus for delivering radioactive emissions in an asymmnetric fashion to target tissue surrounding a surgical extraction site. The apparatus includes an expandable outer surface element defining an apparatus spatial volume, a radiation source disposed within the apparatus volume, and a means for providing predetermined asymmnetric isodose profile within the target tissue.

In one configuration, asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a

longitudinal axis of the apparatus. In one example of an apparatus having this configuration, an inner volume containing a liquid radioisotope is asymmetrically placed within the apparatus volume so as to result in an isodose profile in the target tissue that is asymmetric about the longitudinal axis of the apparatus.

In another example, the radiation source comprises a plurality of spaced apart solid radioactive particles disposed within the apparatus volume and arranged to provide a predetermined asymmetric isodose curve within the target tissue. In one particular example, the plurality of spaced apart radioactive particles are provided on a single elongate member that is shaped so that some of the radioactive particles are farther from the longitudinal axis of the apparatus than others. In other particular examples, a plurality of members carrying radioactive particles are provided with at least one of the members being shaped so as to place at least one radioactive particle asymmetrically with respect to the longitudinal axis of the apparatus.

An interstitial brachytherapy apparatus of the invention may also be implemented in a device having an expandable outer surface defining an apparatus volume, a radiation source disposed within and spaced apart from the expandable outer surface, and at least one asymmnetric radiation shield spaced apart from the radiation source, the asymmetric radiation shielding resulting in predetermined asymmetric isodose curves with in the target tissue. In one embodiment, radiopaque shielding is provided on a portion of the expandable outer surface. In another embodiment, the radiation source is encompassed within a second, inner surface within the apparatus volume, with radiopaque shielding provided on at least a portion of the inner surface. In still further embodiments, one or more radiation shields are spaced apart from the radiation source and within the apparatus volume to achieve the desired asymmetric isodose distribution within the target tissue.

The invention also provides a method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location. The method includes surgically creating access to the proliferating tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue. An interstitial brachytherapy apparatus for delivering radioactive emissions as described above is then provided and intra-operatively placed into the resection cavity. After a prescribed absorbed dose has been delivered to tissue surrounding the apparatus, the apparatus is removed. The radioactive source material may be placed into the interstitial brachytherapy apparatus after the apparatus is placed in the resection cavity, and may be removed before the apparatus is removed. The method has particular applications to brain and breast cancers.

## DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. **1** is a side view of an interstitial brachytherapy apparatus of the invention for delivering asymmetric radioactive doses to body tissue;

FIG. **2** is a cross-sectional view taken along the line **2**—**2** in FIG. **1**;

FIG. **3** is a side view of an additional embodiment of an interstitial brachytherapy apparatus of the invention;

FIG. **3**A is an end view of the interstitial brachytherapy apparatus of FIG. **3**;

FIG. **4** is a side view of an additional embodiment of an interstitial brachytherapy apparatus of the invention;

FIG. **5** is a side view of an interstitial brachytherapy apparatus of the invention configured for use with a liquid radiation source.

FIG. **6** is a side view of an interstitial brachytherapy device of the invention employing radiopaque coatings;

FIG. **7** is a side view of an interstitial brachytherapy device of the invention employing radiopaque coating and a liquid radiation source; and

FIGS. **8** and **9** are end views of interstitial brachytherapy devices of the invention employing radiopaque shields.

## DESCRIPTION OF THE PREFERRED EMBODIMENT

A surgical instrument **10** for providing radiation treatment to proliferative tissue in a living patient is illustrated in FIG. **1**. Surgical instrument **10** includes a tubular body member **12** having first and second lumens **14** and **16** (FIG. **2**) extending from proximal ports **18** and **20** in a molded hub **22**. The first lumen **14** carries a radioactive source **24** and second lumen **16** communicates with inflation port **26** formed through the side wall of the tube **12**.

Affixed to the tubular body **12** proximate the distal end **28** thereof is an outer spatial volume **30** defined by an outer polymeric film barrier **32** that is appropriately spaced from the radioactive source **24**. Outer volume **30** encompasses inflation port **26**. With no limitation intended, the distensible polymeric film walls may comprise a biocompatible, radiation resistant polymer, such as silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, or PVC. The outer spatial volume **30** may be filled with air, saline or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. Alternatively, the surface of outer volume **30** need not be a solid material. For example the surface of the outer volume **30** could be an expandable cage formed from a shape memory metal, such as nitinol, or a suitable plastic, such as an expandable polyethylene cage. Such a cage can be formed in the desired shape to conform to a particular isodose profile, contracted for delivery to the target site in vivo, then expanded to cause the tissue surrounding the surgically resected region to take the appropriate shape. The size of the outer spatial volume **30** generally will correspond approximately to the amount of tissue resected. For some applications, the size of the outer spatial volume **30** may be slightly smaller than the resected volume while for other applications, the outer spatial volume will be slightly larger than the resected volume, allowing the expandable surface of the outer spatial volume to urge tissue on the surface of the resected region into the appropriate shape to promote an even dose distribution around the outer spatial volume in the target tissue. In typical applications, the outer spatial volume has a diameter of approximately 2 to 6 centimeters.

Radiation source **24** comprises a wire **34** having one or more solid radioactive particles **36** located on the wire **34**. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used as the solid radioactive particles. Such a solid radioactive particle configuration offers an advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources. Examples of

radioactive materials which can be selected by a person of ordinary skills in the art for use with the present invention may be found in Tables 1 to 4 of PCT Publication WO 97/19723, which is hereby incorporated by reference.

The, radioactive source **24** can either be preloaded into the catheter at the time of manufacture, or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. If loaded after implantation, the solid radiation emitting material **36** can be inserted through lumen **14** on a wire **34**, for example using an afterloader (not shown).

Radiation source **24** has an asymmetric configuration with respect to a longitudinal axis **38** of the instrument **10**. That is, radiation source **24** is shaped so as to result in an isodose profile **40** that varies radially about the longitudinal axis **38**. More simply, the isodose profile **40** of FIG. **1** has a shorter radius from the longitudinal axis **38** on the top side of the instrument **10** as shown in FIG. **1** than on the bottom side. The asymmetrically shaped isodose curve **40** may be created by providing a plurality of solid radioactive particles **36** on a curved wire **34** in a spaced apart relationship. This configuration will result in certain of the solid radioactive particles **36** being farther from the longitudinal axis **38** of the instrument **10** than others, and will result in the illustrated asymmetric isodose profile **40**. One way to provide the illustrated radioactive source **24** configuration is to form wire **34** from a solid or tubular shape memory alloy such as nickel-titanium alloys known in the art to have such properties. Wire **34** can then be preformed to the desired shape, can be compressed into a substantially straight configuration to pass through lumen **14**, and will resume its desired shape once inside volume **30** where wire **34** will be free from steric constraints imposed inside the lumen **14**. The resulting asymmetric isodose curve **40** can be further tailored by using solid radioactive particles **36** having differing specific activities to achieve the desired dosing.

In,one embodiment, volume **30** and barrier **32** act to separate target tissue from the radiation source **24**. Ideally, radiation therapy should make use the inherent difference in radiosensitivity between the tumor and the adjacent normal tissues to destroy cancerous tissue while causing minimal disruption to surrounding normal tissues. At high doses of radiation, however, the percentage of exposed cells that survive treatment decreases with first-order kinetics in proportion to increasing radiation dose. With increasing cell death comes increasing risk of necrosis or tissue death in healthy tissue that is treated with a high dose of radiation. Accordingly, it is desirable to keep the maximum radiation dose delivered by the brachytherapy apparatus as low as possible while still delivering the desired therapeutic dose to the desired range of tissue. One method for achieving this result is to provide a "hotter" radiation source in a spaced apart relationship to the target tissue. In this way, because the intensity of the radiation emitted by a source drops with the square of the distance from the source, the effective dosage may be maintained below necrosis levels in target tissue closest to the interstitial brachytherapy apparatus while providing the required dosage to a greater depth into the target tissue. (See, e.g., U.S. Pat. No. 5,913,813 which is hereby incorporated by reference in its entirety.) The capability of the apparatus of the invention to deliver absorbed doses deeper into the target tissue than prior interstitial brachytherapy devices while controlling the dose in proximity to the apparatus to reduce or eliminate the risk of healthy tissue necrosis allows for the use of brachytherapy in a greater number of cases.

For example, it is desirable to provide an interstitial brachytherapy device configured to provide a dose in a therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall. In a typical embodiment, the radioactive source material ranges from approximately 150 to 450 mCi in activity and encompasses most of the target treatment area with a 0.4 to 0.6 Gray/hour isodose contour. At this treatment rate, treatment may be completed in approximately 3 to 7 days, or more commonly, in approximately 3 to 5 days.

In some applications, the desired dosing profile is consistent with the shape of the outer volume **30**. That is, the absorbed dose within the target tissue at points equidistant from the surface **32** of the outer spatial volume **30** should be substantially uniform in substantially every direction. Put another way, the three dimensional isodose profiles generated by the radiation source should be substantially similar in shape to the outer spatial volume **30**. Where the apparatus of the invention is deployed in soft tissue, it may also be important for the surface **32** of the outer spatial volume **30** to be sufficiently firm so as to force the target tissue to take on the shape of the surface **30** so that the desired relationship between the isodose profiles and the target tissue is achieved

While the interstitial brachytherapy device **10** of FIG. **1** may employ these techniques to positive effect, this device specifically alters the isodose profile for applications where particularly sensitive tissue or other concerns result in a desire to limit the dosage on one or more sides of the device as illustrated by isodose curve **40**.

In a further embodiment of the brachytherapy device **50** of the invention, illustrated in FIG. **3**, three solid radiation particles **52** are provided in a linear portion **54** of radiation source **56**, while two additional radiation particles **52** are provided on co-planar extending portions **58**, **60** of radiation source **56**. An end view of the device **50** of FIG. **3** is shown in FIG. **3**A with extending portions **58**, **60** provided in a single plane **62**, and resulting in isodose profile **64**. A second inner, expandable surface **66** can also be provided within outer surface **68**; the inner surface **66** enclosing the entirety of radiation source **56**.

By providing extending portions **58**, **60** having radioactive particles in the indicated co-planar relationship, areas of reduced dosage can be created on opposed sides of the device while maintaining symmetric dosing in all other directions. Of course, the number of sources and their configuration can be changed to create a desired asymmetric dosage. For example, an additional source could be added, for example above plane **62**, to result in a symmetric isodose profile in all directions except the direction below the plane **62** which would have a lower dosage.

An additional device **80** of the invention, shown in FIG. **4**, includes a radiation source **82** that is made up of three wires **84**, **86**, **88**, each having a plurality of solid radiation particles. Wire **86** is a straight wire extending along the longitudinal axis **90** of the device, while wires **84**, **88** each curve as wire **34** described above with respect to FIG. **1**. Wires **84**, **88** are coplanar, resulting in an isodose profile **92** that is similar to isodose profile **64** of FIG. **3**A. That is, the isodose profile will be symmetric in the plane in which the wires **84**, **88** are disposed, but will have areas of reduced dosage in directions transverse to that plane (i.e., in FIG. **4**, in the directions into and out of the page). As with the device **50** of FIGS. **3** and **3**A, device **80** can be configured with more or fewer wires **84**, **86**, **88**, and can be provided in configurations other than the depicted co-planar configuration in order to achieve desired asymmetric isodose profiles.

The asymmetric dosing effect achieved by the devices described above can also be achieved using a liquid radiation source. For example, device **100**, illustrated in FIG. **5**, has an outer surface **102** defining an outer volume **104** and an inner surface **106** defining an inner volume **108**. The inner surface **106** is asymmetrically shaped or located with respect to the longitudinal axis **110** of the device **100** so as to result in the desired asymmetric dosing when the inner volume **108** is filled with a radioactive fluid. The inner volume **108** is spaced apart from the outer surface **102** and can be filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material contained within the inner volume **108** can be a fluid made from any solution of radionuclide(s), e.g., a solution of Ir-192, I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel. One radioactive material useful in the invention is Iotrex™, a sterile single use, non-pyrogenic solution containing sodium 3-($^{125}$I)iodo-4-hydroxybenzenesulfonate ($^{125}$I-HIBS), available from Proxima Therapeutics, Inc. of Alpharetta, Ga. The inner volume **108** may be filled with radioactive fluid through port **112**. Similarly, outer volume **104** can be filled on inflated using port **114**.

A desired asymmetric dosing profile having the dosing characteristics described above may also be created by using asymmetric shielding between the radiation source and the target tissue as illustrated in FIGS. **6** through **9**. In the device **120** of FIG. **6**, a balloon **122** is located on the distal end of catheter **124**. Radioactive particles **126** are disposed along the longitudinal axis **128** of the device. A portion of the surface, either inner or outer, of balloon **122** is coated with a radiopaque material **130** to result in asymmetric isodose curve **132**. Radiopaque materials suitable for coating onto a polymeric surface of balloon **122** include, for example, barium, tungsten, bismuth, tantalum and tin.

A further device **140** having radiopaque shielding **142** is illustrated in FIG. **7**. Device **140** includes an outer volume surface **144** and an inner volume surface **146**. Inner surface **146** may contain a liquid radiation source, or may enclose one or more solid particles as used in device **120** (FIG. **6**). In device **140**, the radiopaque material **142** is coated onto a portion of either the inner or outer side of the inner volume surface **146**, resulting in a desired asymmetric isodose profile **148**.

Additional devices **160**, **180** of the invention having radiation shielding **162** are illustrated in FIGS. **8** and **9**, respectively. In these devices **160**, **180**, one or more radiation shields **162** are provided between and spaced apart from a radiation source (not shown) located along a longitudinal axis **164** of the device and the target tissue, which will be located outside of expandable surface **166**. The radiation source can include a liquid or a solid radiation source as described above. Shields **162** can be formed from radiopaque materials including those described above with respect to the radiopaque coating and can extend longitudinally from a base on the device located within the expandable surface **166**.

As shown in FIG. **8**, device **160** has two radiation shields **162** on opposed sides of catheter **168**. This configuration results in lower radiation dosing on the two sides of the device **160** on which the shields **162** are located as shown by isodose curve **170**. Device **180** (FIG. **9**) has a single radiation shield **162** resulting in an asymmetric isodose curve **182** as shown. A person or ordinary skill in the art will recognize that other configurations may be employed to achieve desired isodose curves.

The interstitial brachytherapy apparatus of the invention can be used in the treatment of a variety of malignant tumors, and is especially useful for in the treatment of brain and breast tumors.

Many breast cancer patients are candidates for breast conservation surgery, also known as lumpectomy, a procedure that is generally performed on early stage, smaller tumors. Breast conservation surgery is typically followed by postoperative radiation therapy Studies report that 80% of breast cancer recurrences after conservation surgery occur near the original tumor site, strongly suggesting that a tumor bed "boost" of local radiation to administer a strong direct dose may be effective in killing any remaining cancer and preventing recurrence at the original site. The apparatus described herein can be used for either the primary or boost therapy. Numerous studies and clinical trials have established equivalence of survival for appropriate patients treated with conservation surgery plus radiation therapy compared to mastectomy.

Surgery and radiation therapy are also the standard treatments for malignant solid brain tumors. The goal of surgery is to remove as much of the tumor as possible without damaging vital brain tissue. The ability to remove the entire malignant tumor is limited by its tendency to infiltrate adjacent normal tissue. Partial removal reduces the amount of tumor to be treated by radiation therapy and, under some circumstances, helps to relieve symptoms by reducing pressure on the brain.

A method according to the invention for treating these and other malignancies begins by surgical resection of a tumor site to remove at least a portion of the cancerous tumor and create a resection cavity. Following tumor resection, but prior to closing the surgical site, the surgeon intraoperatively places an interstitial brachytherapy catheter apparatus, having an inner spatial volume and an outer spatial volume as described above but without having the radioactive source material loaded, into the tumor resection cavity. Once the patient has sufficiently recovered from the surgery, the interstitial brachytherapy catheter is loaded with a radiation source. The radioactive source dwells in the catheter until the prescribed dose of radiotherapy is delivered, typically for approximately a week or less. The radiation source is then retrieved and the catheter is removed. The radiation treatment may end upon removal of the brachytherapy apparatus, or the brachytherapy may be supplemented by further doses of radiation supplied externally.

It will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention, including, but not limited to, combinations of elements from different embodiments found herein. All references cited herein are expressly incorporated by reference in their entirety.

What is claimed is:

**1**. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume.

**2**. A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.

**3**. The apparatus of claim **2**, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.

**4**. The apparatus of claim **3**, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.

**5**. A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.

**6**. A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.

**7**. The apparatus of claim **6**, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.

**8**. The apparatus of claim **1**, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.

**9**. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source disposed completely within and spaced apart from the expandable outer surface; and

an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume.

**10**. The apparatus of claim **9**, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.

**11**. The apparatus of claim **10**, wherein the expandable outer surface comprises an inflatable balloon.

**12**. The apparatus of claim **11**, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.

**13**. The apparatus of claim **9**, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.

**14**. The apparatus of claim **13**, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.

* * * * *

K071229

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## 5. 510(K) SUMMARY

| | |
|---|---|
| **Prepared date** | April 20, 2007 |
| **510(k) owner** | **SenoRx, Inc.**<br>11 Columbia<br>Aliso Viejo, CA 92656<br>P. 949.362.4800 F. 949.362.3200 |
| **Contact person** | Eben Gordon |
| **Device name** | SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy |
| **Common name** | Multi-lumen balloon source applicator |
| **Classification name** | Remote controlled radionuclide source applicator |
| **CFR classification** | 21 CFR 892.5700 90 JAQ |
| **Predicate device** | Adjustable Multi-Catheter Source Applicator (K062241)<br>MammoSite Radiation Therapy System (K041929) |
| **Decision date** | 11/9/2006 (K062241)<br>8/26/2004 (K041929) |
| **Device description** | The SenoRad applicator consists of a multi-lumen catheter connected to an inflatable spherical balloon that can be attached to commercially available High Dose Rate remote afterloader equipment for passage of the radiation source delivery wire. Five radiation source wire lumens are provided; one central lumen located along the long axis of the applicator and four curved lumens symmetrically offset from the central lumen. The balloon is inflated to a 4 or 5 cm spherical shape by a controlled volume injection of physiological saline to approximately 32 or 55 ml, respectively. |
| **Indications for use** | The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer. |
| **Summary of substantial equivalence** | Extensive preclinical testing was conducted to evaluate and characterize the performance of the SenoRad Multi-Lumen Balloon Source Applicator. Preclinical studies conducted included in vitro laboratory studies to demonstrate that the SenoRad applicator performed as intended under simulated use conditions. Biocompatibility testing was performed to |

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demonstrate that the materials meet ISO 10993-1 requirements. The dosimetry of the SenoRad applicator was characterized. Based on these findings, it was concluded that the SenoRad applicator could deliver an equivalent radiation dose as the current brachytherapy applicators.

The SenoRad applicator has the following similarities to the previously cleared predicate devices: same indications for use; same intended use; same intended treatment site; same operating principle; same technological characteristics; equivalent dosimetric characteristics; and same sterilization method. The materials of construction vary in a manner that has no impact on device safety.

In summary, the SenoRad Multi-Lumen Balloon Source Applicator as described in this submission is substantially equivalent to the predicate devices.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
9200 Corporate Blvd.
Rockville MD 20850

MAY 18 2007

SenoRx, Inc.
% Mr. Mark Job
Responsible Third Party Official
Regulatory Technology Services LLC
1394 25th Street NW
BUFFALO MN 55313

Re: K071229
Trade/Device Name: SecoRad Multi-Lumen Ballon Source Applicator for Brachytherapy
Regulation Number: 21 CFR §892.5700
Regulation Name: Remote controlled radio-nuclide applicator system
Regulatory Class: II
Product Code: JAQ
Dated: May 2, 2007
Received: May 3, 2007

Dear Mr. Job:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at one of the following numbers, based on the regulation number at the top of this letter:

| | | |
|---|---|---|
| 21 CFR 876.xxx | (Gastroenterology/Renal/Urology | 240-276-0115 |
| 21 CFR 884.xxx | (Obstetrics/Gynecology) | 240-276-0115 |
| 21 CFR 894.xxx | (Radiology) | 240-276-0120 |
| Other | | 240-276-0100 |

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150
or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Nancy C Brogdon

Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

## 4. INDICATIONS FOR USE

510(k) Number (if known): K071229

Device Name: _____ SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy _____

Indications for Use:

The SenoRad Multi-Lumen Balloon Source Applicator for Brachytherapy is intended to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.

Prescription Use ___X____ AND/OR Over the Counter Use _____

(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Nancy C Brogdon

(Division Sign-Off)
Division of Reproductive, Abdominal, and Radiological Devices
510(k) Number K071229

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